Neurology

OFFICIAL JOURNAL OF
THE AMERICAN ACADEMY OF NEUROLOGY

DECEMBER--1956

Volume 6 — Number 12

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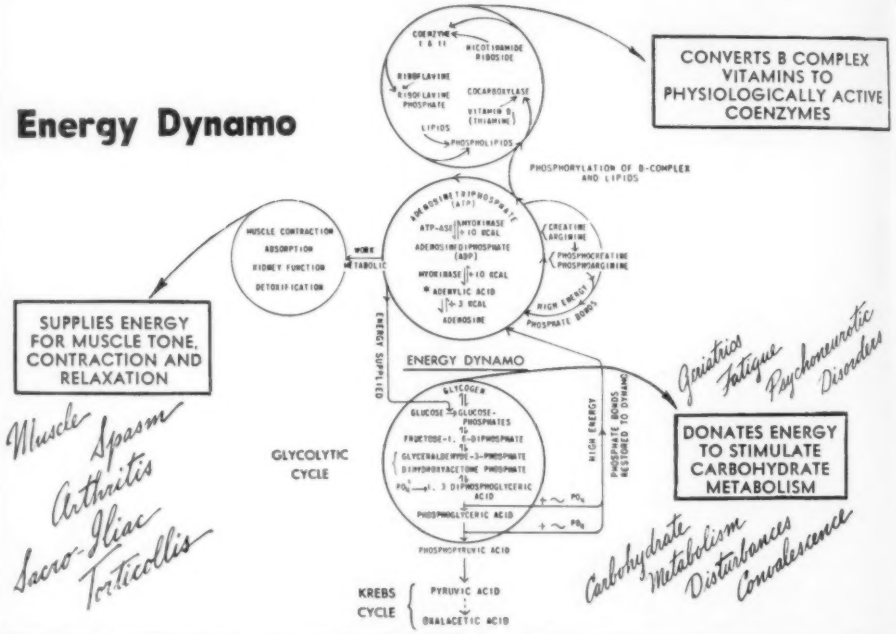

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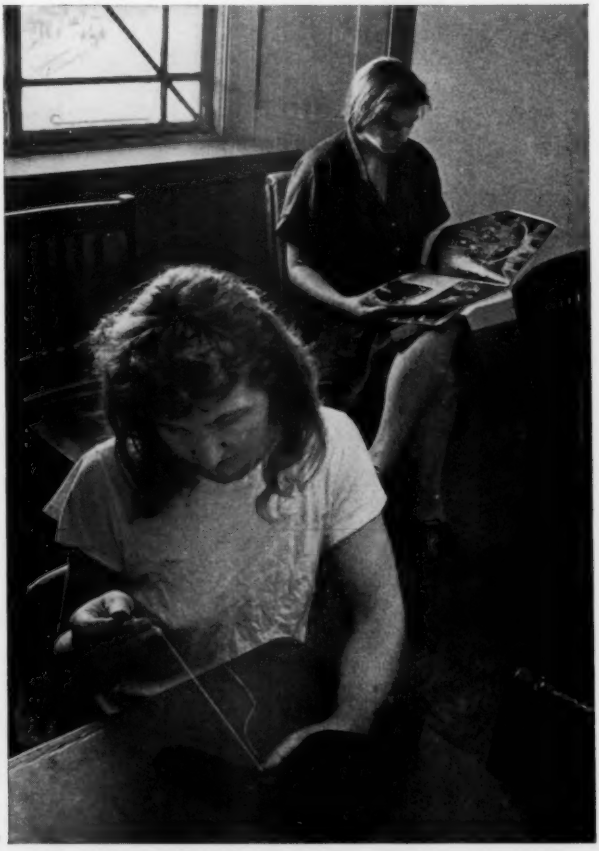

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1. Livingston, S., and Petersen, D.: New England J. Med. *254*:327 (Feb. 16) 1956.
2. Pence, L. M.: Texas State J. Med. *50*:290 (May) 1954.
3. Berman, B. A.: Am. J. Psychiat. *112*:541 (Jan.) 1956.

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INFORMATION FOR *Authors*

NEUROLOGY, the official publication of the American Academy of Neurology, has been instituted to provide a medium for prompt publication of articles dealing with neurology and its cognate fields and to stimulate individual investigation in these various fields.

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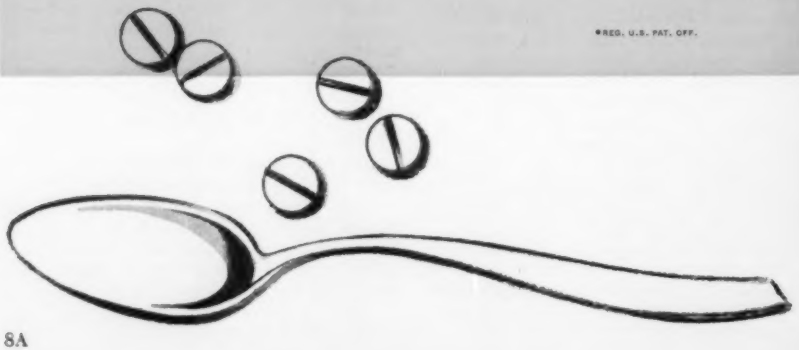

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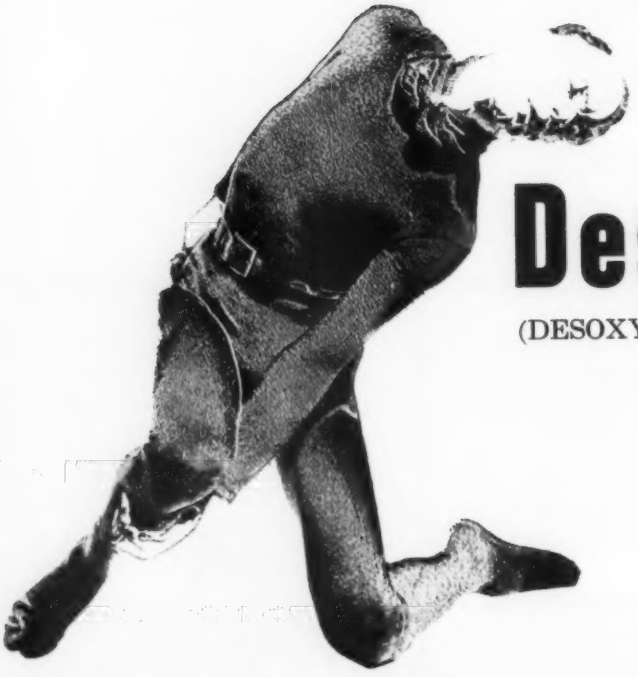

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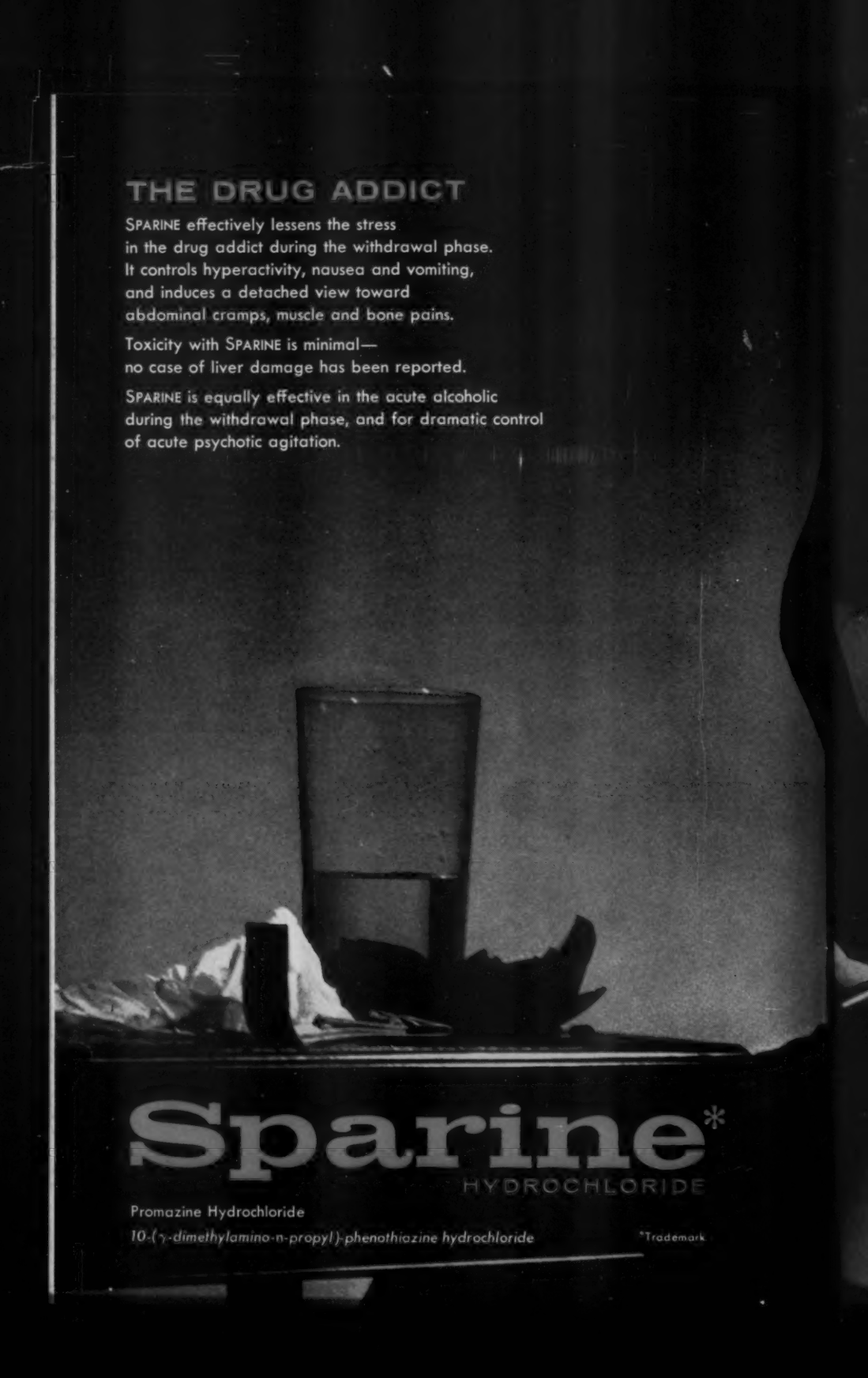
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Volume 6 Neurology Number 12

Large Intracranial Aneurysm Producing Panhypopituitarism and Frontal Lobe Syndrome

Philip G. Gallagher, M.D., Joseph F. Dorsey, M.D., Mario Stefanini, M.D. and Joseph M. Looney, M.D.

MORGAGNI AND BIUMI are credited with describing intracranial aneurysms in 1761 and 1765, respectively.[24,25] Since that time there have been many reports, at first concerned with the intracranial aneurysm as a pathologic curiosity found only at autopsy, while more recently it has become a clinical problem of the neurosurgeon. The purpose of this paper is to present and discuss a case recently observed at our institution and believed to be the largest intracranial aneurysm reported. It was proved by arteriography, along with sufficient clinical and laboratory evidence of pituitary dysfunction and frontal lobe destruction.

CASE REPORT

A 54 year old white married housewife was first seen at this hospital on July 10, 1955, with the complaint of headache. The patient had suffered from periodic migrainous and right-sided headaches for the past 20 years. Nine years prior to admission she noted that reading might precipitate the severe headaches. She was seen by her physician at that time and treated for hypertension and anemia. Eight years prior to admission the patient developed blurring of vision and periodic inward deviation of the right eye. Her blood pressure was reported to be variable during this time, ranging from 170/100 to 100/60. During the past few years she complained of polyuria and frequency.

Six weeks prior to admission the patient became very weak, lost weight in spite of good appetite, and spoke only in a mumble. On the day before admission there was sudden loss of vision in the right eye and weakness of the left side of the body. She was brought to a hospital where she was found to be semistuporous and to have difficulty in understanding and responding to commands.

Physical examination revealed a pale, thin, apprehensive, chronically ill female appearing much older than her stated age (figure 1). Her skin and scalp hair were dry and coarse. Breasts were atrophic. There was striking absence of the outer portion of both eyebrows and total

From the neurosurgical service and Joseph Stanton Research Laboratory, St. Elizabeth's Hospital; the departments of surgery and medicine, Tufts University School of Medicine; and the department of biochemistry, Boston University School of Medicine, Boston.

Read at the eighth annual meeting of the American Academy of Neurology, St. Louis, April 27, 1956.

FIG. 1. Appearance of patient before and after occurrence of symptoms. *A*, ten years prior to hospital admission; *B*, at time of admission.

body hair. The right lid was ptotic; right eye was totally blind and deviated inward. The right pupil did not respond to direct stimulation by light, yet consensual reaction from left to right was present. The right optic disk was completely atrophic. Only minimal medial, upward, and downward movements were possible in the left eye, while lateral movements were absent. The left optic disk was normal. The fields were full to confrontation testing on the left. She was able to read sub-headline size type with that eye. The mouth drooped slightly to the right and the tongue deviated moderately to that side. The patient had poor muscular development and decreased motor power especially on the left; no essential change in sensation was present. Deep tendon reflexes were hypoactive, while abdominal and ankle jerks were absent. Plantar reflex was flexor on the right and absent on the left. Finger-to-nose test was fairly well performed. The patient had a tendency to fall backward and to the left from the Romberg position and there was staggering and swaying to the left. During the course of physical examination she would display lethargy, then apprehension; she was fearful of being hurt, was restless. There was difficulty in holding the patient's attention. She was easily distracted and had alternating moods of elation and depression, paranoid delusions and hallucinations, memory lapses, confusion, and tendency toward repetition. She was very fearful of being alone. The remainder of the physical examination was not remarkable.

Hospital course. A lumbar puncture revealed normal pressure; it yielded clear fluid containing two white blood cells per high power field and normal protein content. Skull films (figure 2) showed complete destruction of the dorsum sellae; the posterior and anterior clinoid processes were eroded, and the floor of the sella turcica appeared destroyed with bilateral pressure erosion of the sphenoidal air sinuses. A poorly defined, thin, curvilinear type of calcification was located anteriorly and posteriorly in relation to the sella. This measures about 5 cm. in its anteroposterior diameter. Two days later the patient had a right cerebral arteriogram under Pentothal anesthesia, after which she did not regain consciousness. Her blood pressure dropped to 80/60 and her respirations were shallow. She received Levophed (*d*) intravenously with a minimal response. On a supposition of pituitary insufficiency causing sec-

FIG. 2. X-ray of skull (lateral view). (*a*) destruction of dorsum sellae; (*b*) erosion of anterior and posterior clinoid processes and body of sphenoid; (*c*) a curvilinear density of calcification, outlined by arrows.
FIG. 3. Arteriogram (right, anteroposterior view). Demonstrates the large aneurysm.
FIG. 4. Arteriogram (right, lateral view). Aneurysm (7.5x5 cm.) originates from internal carotid artery near the bifurcation of anterior and middle cerebral arteries.
FIG. 5. Ateriogram (left, lateral view). Demonstrates displacement of the left carotid artery by aneurysm of the right internal carotid artery.

ondary hypoadrenalism, the patient was started on 50 mg. of cortisone per day with improvement. She then was placed on 40 mg. of ACTH gel and ½ gr. of thyroid extract daily, and continued to improve.

The right cerebral arteriogram (figure 3) demonstrated that the parasellar portion of the right internal carotid artery was 3 cm. lateral to the midline (figure 4). The vessel could be followed to a point above the anterior clinoids, beyond which the opaque media passed into a mass, 7.5 cm. wide and 5 cm. deep. The aneurysm appeared to be arising from the internal carotid artery near the bifurcation of the anterior cerebral and middle cerebral arteries.

Injection of the left internal carotid artery (figure 5) revealed displacement of the vessel in the region of the sella—most likely due to the aneurysm of the right internal carotid, but there was no evidence of communication between the right and left sides.

On the eighth hospital day, under local anesthesia, the right common carotid artery was tied to tolerance of three-quarters occlusion.

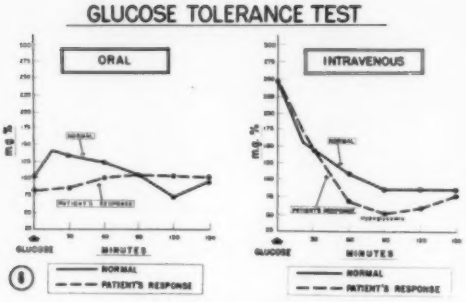

FIG. 6. Glucose tolerance test. (*a*) flat oral glucose tolerance curve; (*b*) marked drop of blood glucose level after intravenous administration of glucose (results are best explained on the basis of lack of glucogenic hormone of the adrenal cortex).

The patient did well postoperatively and suffered no further neurologic changes. Pre- and postoperatively she received supplementary cortisone, thyroid, and sodium chloride.

When the patient's over-all condition improved, all therapy was stopped and endocrinologic evaluation was carried out (table 1). An ACTH test of Thorn was performed. A single dose of ACTH (10 mg. i.m.) resulted in no change in circulating eosinophils or urinary uric acid/creatinine ratio. The test was extended to a 48 hour period. After stimulation of the adrenal with ACTH for 48 hours, a fall of circulating eosinophils of 59 per cent resulted. The urinary excretion of 17-ketosteroids rose from 1.2 mg. per 24 hours to the normal range of 10.8 mg. per 24 hours. This response was considered to be consistent with panhypopituitarism. The protein-bound iodine was never higher than 3.5 gamma per cent. No follicle stimulating hormone was present in the urine at any time. Oral glucose tolerance test revealed a flat curve which was interpreted as indicating delayed absorption by the gastrointestinal tract. During the intravenous glucose tolerance test, blood glucose dropped to a low level (50 mg. per cent in 90 minutes), at which level the patient showed clinical signs of hypoglycemia. A temperature of 102° F. developed several hours later. This result duplicates that found in adrenal insufficiency states as a result of poor availability of adrenocortical glucogenic hormone (figure 6).

The patient's electrolytes showed a marked tendency to hyponatremia. It was interesting to correlate variations of serum sodium level with therapy (figure 7). The patient showed a tendency to low serum sodium (in the range of 120 meq/L.). On treatment with cortisone, thyroid, and sodium chloride, serum sodium

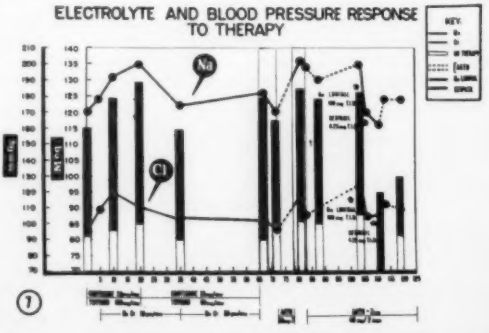

FIG. 7. Electrolyte and blood pressure response to therapy. (*a*) temporary elevation of serum sodium and chlorides level and of arterial pressure following high doses of cortisone and thyroid extract (day 0-20); (*b*) return to original values of these constituents after reduction of dose of cortisone and thyroid extract (day 21-35); (*c*) elevation of serum sodium level and systolic pressure when higher doses of NaCl were administered (day 36-65); (*d*) prompt return of serum sodium level and systolic blood pressure to original values after discontinuation of all therapy (day 66-71); (*e*) rise of serum sodium level and of arterial blood pressure on institution of ACTH therapy (day 71-86), stabilized by administration of long acting ACTH-zinc prepaartion (day 82-125); (*f*) prompt drop in serum sodium level with administration of sodium Luminal (day 104); (*g*) prompt drop in arterial pressure and further, slight drop in serum sodium level following administration of Serpasil (day 105).

TABLE 1
ENDOCRINE PATTERN OF PATIENT M. Y.

Test	*Result*	*Normal*
Protein bound iodine	3.5 (gamma per cent)	4—8
Follicle stimulating hormone	0 (dil. 5-200) mg./24 hours	+(dil. 5-10) Av. mg./ 24 hours
17-hydroxycorticosteroids	0.4	3.8
17-ketosteroids	1.2	11.0
17-ketosteroids	3.2 (25 mg. ACTH)	
17-ketosteroids	5.1 (10 mg. ACTH q 6°—24 hours)	
17-ketosteroids	10.8 (10 mg. ACTH q 6°—48 hours)	

(a) low protein-bound iodine; (b) absence of FSH excretion; (c) low steroid urinary excretion and its striking improvement after administration of ACTH.

and chloride levels and blood pressure tended to rise. Fear of rupture of the aneurysm through increased intracerebral arterial pressure advised restriction of cortisone and thyroid dosage. A definite response was obtained, since serum sodium and arterial pressure returned to the original range. By increasing the intake of sodium chloride from 10 to 20 gm. per day, a gradual rise in blood pressure and serum sodium again occurred while chlorides remained essentially unmodified. On day 65 all therapy was stopped. Within a five-day period serum sodium and chloride levels and blood pressure dropped to the original values. Administration of 10 units of ACTH i.m. every six hours for a period of 48 hours induced a marked rise in serum sodium, chlorides, and arterial blood pressure. The patient then was stabilized on long-acting corticotrophin zinc.

An interesting finding was noted on the 104th hospital day when, due to the rising blood pressure, small doses of sodium Luminal (100 mg. t.i.d.) were administered. Within a few hours serum sodium dropped from 136 to 120 meq/L. and serum chlorides from 98 to 86 meq./L. Administration of Serpasil reduced further the serum sodium level to 116 meq./L. while blood pressure dropped to 108/70. Upon suspension of Serpasil administration and without any change in ACTH dosage, electrolytes and blood pressure returned to the previous level.

Additional laboratory data are shown in table 2. These were essentially normal.

DISCUSSION

The etiology, pathology, and clinical symptoms of intracranial aneurysms have

TABLE 2
ADDITIONAL LABORATORY DATA IN PATIENT M. Y.

RBC—3.52 M. cu.mm. Hct.—34. Hgb.—11.3 gm.

WBC—10,000; 77 polys; 3 bands; 7 lymphs; 3 atyp. lymphs; 1 mono; 9 eos.

ESR.—60 mm./1 hr. (Westergren).

Bone marrow—increased megakaryocytes.

Urine—yellow; alkaline. S.G. 1.006. Daily urinalysis showed consistently low specific gravity in the range of 1.007.

Total serum protein—6.3 gm. per cent; albumin 3.4 gm. per cent; globulin 2.9 gm. per cent.

Serum electrophoresis—increased alpha 2 fraction.

Cholesterol—206 mg. per cent. Esters 112 mg. per cent.

Hinton—negative.

Chest x-ray—negative.

EKG—within normal limits.

EEG—16 leads with hyperventilation. Dominant rhythm well modulated alpha activity of moderate amplitude. Minimal slowing (Theta) in the right occipito-parietal region. (There was no change in the EEG after ligation of the common carotid artery).

Acid fast studies—negative.

been adequately covered by many authors.[2–5,11,13] Comments will be directed primarily to some pertinent findings of our case which are of interest from a physiologic and pathologic point of view. The aneurysm of our patient apparently arose from the internal carotid artery near the bifurcation of the middle cerebral and anterior cerebral arteries. Aneurysms of this portion of the artery seldom reach a size of more than 1 cm. Since the aneurysm we discuss is the largest one proved by arteriography and reported thus far, the comparison already emphasizes the interest of the case. Also, amazingly enough, we found no evidence of aneurysmal rupture or leak in our patient, while patients with much smaller aneurysms usually present early intracranial bleeding.[2,3,13,14]

The localizing signs and symptoms of our patient could be explained by the impinging of the aneurysm upon the second, third, fourth, and sixth cranial nerves, the tips of the temporal lobes, the pituitary body, and the frontal lobes. In view of the extensive bone destruction seen in the region of the sella turcica, it is logical to assume that the resulting damage was of progressive nature, yielding a relatively gradual onset of symptoms and irreparable neurologic signs. Predominance of visual disturbances in our patient was not surprising. Dandy[11] and Jefferson[12] found loss of vision and primary optic atrophy to be the outstanding symptoms of cases having diffuse dilatation of the carotid trunk. The finding of periodic headache, often a migrainous type, in association with ophthalmoplegia is not unusual in patients with intracranial aneurysms.[3,15] It has been suggested that this phenomenon is due to abnormal relationships of the internal carotid artery to the oculomotor nerve, the vascular derangements distorting the nerve and thus producing the attacks.[9,15]

THE PITUITARY SYNDROME

Aneurysms impinging upon the pituitary gland have been reported.[6,7,10,13] However, this is the first case in which dysfunction of the gland has been proved to be related to pressure by an unruptured intracranial aneurysm. An aneurysm as large as found in our patient acts as any space-occupying lesion. thus causing partial or complete atrophy of the pituitary gland, resulting in panhypopituitarism.[1,16] Hypothyroidism, as we observed in the patient, is usually part of the clinical picture of panhypopituitarism. Its symptoms are clinically indistinguishable from those of primary hypothyroidism. Yet this distinction is very important not only from a viewpoint of differential diagnosis, but because thyroid medication in patients with hypothyroidism due to pituitary deficiency may precipitate an adrenal cortical crisis. This is explained by the ability of thyroid extract to enhance sodium, chlorides, and water excretion.[16] The existence of hypopituitarism in the patient could hardly be doubted on the evidence of clinical (atrophy of the breasts, scanty body hair, and so on) and laboratory findings (normal cholesterol level, sensitivity to insulin, absent follicle stimulating hormone, low protein-bound iodine, low urinary 17-ketosteroids, and hydroxycorticosteroids). The 48-hour ACTH test also supported this diagnosis. After 48 hours of stimulation with ACTH, the activated secretions of the adrenal cortex (compounds E and F) depressed the circulating eosinophils by 59 per cent and caused a considerable rise in the urinary excretion of 17-keto-

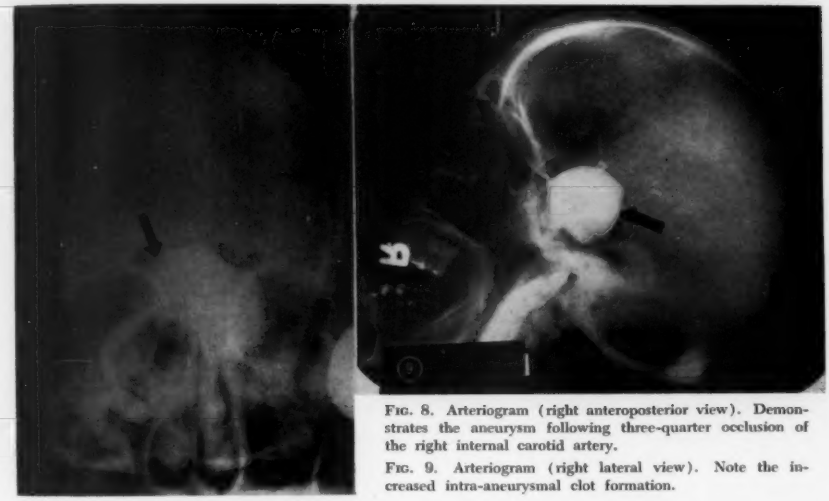

FIG. 8. Arteriogram (right anteroposterior view). Demonstrates the aneurysm following three-quarter occlusion of the right internal carotid artery.

FIG. 9. Arteriogram (right lateral view). Note the increased intra-aneurysmal clot formation.

steroids. Thus, in our patient, the adrenocortical tissue was not in a state of primary atrophy but only of temporary hypofunction due to lack of stimulation by endogenous ACTH.[1,16,17,21] Due to the size of the aneurysm, some of the signs and symptoms observed might have been attributed to hypothalamic involvement. Clinical and experimental evidence points to the hypothalamus in the physiology of carbohydate, fat, and water metabolism. The hypothalamicoadenohypophyseal relationships in endocrinopathies are well established, and it is extremely difficult to attribute functions of the latter, excluding the influence of the former.[16] We found it most interesting that sodium Luminal and Serpasil resulted in such a marked sodium drop (figure 7). Both of these drugs have a common denominator, that is, sedation. The exact localization of action of either in the central nervous system has not been proved, but has been attributed to the hypothalamus.[18] It will be of interest to continue studies along this line in relation to the various "cerebral salt syndromes."

We have not proved diabetes insipidus in our patient. It has been shown experimentally that diabetes insipidus requires bilateral destruction of the supraoptic nuclei, or removal of the posterior lobe of the pituitary gland or its stalk. The presence of the anterior lobe of the pituitary and of the thyroid appear to be necessary for diabetes insipidus to occur. It is also worth mentioning that even when diabetes insipidus is present, spontaneous recovery often occurs.[16]

The large intracranial aneurysm has impinged upon the frontal lobes of the brain. Extensive prefrontal destruction produces the so-called "frontal lobe syndrome,"[22,23] the symptoms of which can be divided into seven groups: 1) lack of restraint leading to boasting, self-aggrandizement, hostility, aggressiveness; 2) distractibility and restlessness—difficulty in fixing attention; 3) flight of

ideas, puerile fantasies, emotional instability, facetiousness, punning; 4) lack of initiative; 5) impairment of memory for recent events, but not for remote events; 6) impairment of moral and social sense, loss of love for family; 7) failure to realize or indifference to the seriousness of one's condition and often a sense of well-being. The exact mechanism of the physiologic processes of the frontal lobes is not fully known. Many relate the function to planning and prudent initiative. The ability to think abstractly and assume a categorical attitude appears to be one of the chief functions of the frontal lobes.[23] We do not like to become involved in the many theories and studies of frontal lobe function. We merely wish to categorize the multiple psychiatric and psychologic evaluations of the patient into one clinical picture. We feel that these are best classified under the broad group of frontal lobe disturbances. Symptoms from ruptured aneurysms in the region of the frontal lobes have been reported,[3] and the mental derangements of cases of large aneurysms reported in the past may well be explained by frontal lobe destruction (Bramwell's case).[9]

Therapeutically, the best course was reparative. The patient has been placed on long-acting corticotropin[19] since adrenal insufficiency was the immediate problem. As a result, the adrenal steroids have been maintained within the normal range. It was also decided to place the patient on a combination of estrogen and androgen (Deladumone)* for its protein sparing and mild salt-retaining effect and symptomatic relief. The patient has continued on thyroid extract.

Three-quarter occlusion of the internal carotid artery has not reduced the size of the aneurysm, but has resulted in intra-aneurysmal clot formation (figures 8 and 9). On good endocrine control the patient has returned to her home, can do small household duties, and has had no progression of her symptoms. The course of further neurosurgical procedures is under deliberation.

SUMMARY

The article discusses a patient with a large intracranial aneurysm originating from the right internal carotid artery. This case appears to represent the largest unruptured intracranial aneurysm, seen in vivo, described. By virtue of its size, the aneurysm effected compression not only of several ocular cranial nerves but also of the pituitary gland and of the frontal lobes of the brain. Compression resulted in symptoms of hypopituitarism with secondary adrenal hypofunction, hypogonadism, and hypothyroidism, along with the development of frontal lobe syndrome. Several experimental observations are discussed.

We are indebted to Dr. Edward J. Healey, Waltham, Massachusetts, for reading the arteriograms. 17-ketosteroid determinations were kindly performed by Dr. Henry M. Lemmon, Associate Professor of Medicine, Boston University School of Medicine.
Determination of follicle stimulating hormone was kindly performed by Dr. Maurice S. Raben, New England Center Hospital, Boston.
The authors wish to acknowledge the valuable contributions to this study of Dr. James Graham, Dr. Peter F. Piccinini and Dr. William Carey, Saint Elizabeth's Hospital, Boston, Massachusetts.
*Supplied by E. R. Squibb & Sons, New York.

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■ Pathological cases show that when there is an alteration in one-half of the spinal cord, the blood vessels in that side are paralyzed, as are also the muscles. There is more blood in these paralyzed parts, and the temperature is higher than it is normally. In the opposite side the reverse obtains. It seems from these facts, and from many experiments, that it is from paralysis of the vasomotor nerves, and from their irritation in the cerebro-spinal axis, that arises the difference of temperature between the two sides of the body, in cases of alteration of a part of one-half of this axis.

C. E. Brown-Séquard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

An Early Description of the Gerstmann Syndrome

Arthur L. Benton, Ph.D. and Russell Meyers, M.D.

In 1924 Josef Gerstmann described "finger agnosia," an apparently hitherto unrecognized behavioral deficit appearing as a consequence of cerebral disease.[1] In this and subsequent papers, he called attention to the frequent association of finger agnosia with right-left disorientation, dyscalculia, and dysgraphia.[2,3] His observations were soon confirmed by other investigators, and the tetrad of symptoms has come to be known as the Gerstmann syndrome.

While right-left disorientation, dyscalculia, and dysgraphia were phenomena that had long been familiar to clinicians, it is generally believed that finger agnosia, that is, the inability to localize fingers subjected to tactual stimulation or to name or otherwise indicate them upon verbal command, was not known before the appearance of Gerstmann's communication. This impression is not altogether correct. In 1888 the French ophthalmologist, Jules Badal, published a detailed case report[4] describing a female patient who, during a considerable period of study following severe eclampsia characterized by edema, convulsions, coma, and anemia, showed a variety of behavioral deficits including finger agnosia and the other elements of the Gerstmann syndrome. Other deficits, sometimes considered to be associated with the syndrome, such as constructional apraxia and spatial and temporal disorientation, were also present.

Badal's case report was evidently not unknown to neurologists 50 years ago. In a monograph published in 1898 Pick quoted rather extensively from it, and in a communication ten years later he referred to it as "the well known case of Badal."[5,6] However, this early contribution appears to have been overlooked in recent years, for it is not mentioned in the reasonably complete historical surveys included in current monographs.[7–10] Hence, it seems worthwhile to recall attention to this once "well known" case report, both as a matter of intrinsic historical interest and because it poses a problem which is still unsettled.

THE CASE OF VALERIE CLEM . . . .

Badal's patient was a 31 year old married woman who entered his clinic in Bordeaux complaining of rather peculiar visual disturbances and exhibiting "a strange combination of bizarre and incoherent phenomena." Her medical history prior to a recent first pregnancy had been unremarkable. The pregnancy itself had

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been uneventful until the eighth month when edema developed, initially involving the lower extremities and progressing rapidly to implicate the thigh and abdomen. One morning she suffered from copious epistaxis, which was followed by four major eclamptic attacks within an hour. At the obstetric clinic, to which she had been brought in an unconscious state, it was noted that the edema was severe, involving the labia and the abdominal wall as well as the lower limbs. The convulsions were controlled after use of chloroform for three hours. Consciousness was regained during the next hour. Variable amounts of albumin (1 to 7 gr./1,000 cc.) were found in the urine during the next week. No visual disturbances were observed.

Eight days after admission she delivered two living female infants, the first weighing 900 gm. and the second, a breech delivery accomplished 90 minutes after the first, weighing 2,200 gm. There was extensive hemorrhage after the birth of the second infant. The edema now receded rapidly. During the following week she showed mild delirium and confusion with hallucinatory activity and occasionally refused food. A paralysis of the left levator palpebrae superioris was apparent and persisted for some eight days. The pupils were dilated and sluggish. Vision appeared to be profoundly disturbed, but ophthalmoscopic examination was negative. At one time during this period she ran a temperature of 104° F. Anemia was severe. Neither motor nor speech difficulty was ever manifested, although a general asthenia was apparent.

The confusional state and the blepharoptosis disappeared, and the patient returned home. However, the visual difficulties persisted during the next six weeks, at the end of which period she entered Badal's clinic. Her principal complaint was visual disorientation. Despite apparently excellent visual acuity, she could not find her way about the house. She had difficulty in locating objects, and when found she would reach past or to the side of them in attempts at apprehension. There was no diplopia, strabismus, or other disturbance of the extraocular movements. The pupils were not considered remarkable and their reactions to accommodation were intact.

Color vision was intact and color naming fluent. Central visual acuity was normal, but perimetric study indicated both a bilateral inferior hemianopsia and significant constriction of both upper visual fields. There was complete loss of topographic orientation. The patient could not find her way about the neighborhood, nor was she able to answer simple questions about the spatial relations of the main streets of Bordeaux although she had long been thoroughly familiar with them.

She could read letters and numbers, but only the simplest and most familiar words. She could not read other simple words and seemed to have lost all sense of directional orientation with respect to the printed material. "She could name isolated characters without difficulty but when several letters were placed, one after the other, she could not follow the order in which they were arranged . . . . It was impossible for her to say whether such and such a letter was placed before or after another and consequently she could not make out the simplest syllable or determine where the line began or ended." She found it quite impossible to spell even those words which she was able to read.

She appeared to have an absolute agraphia. She could not write, either from dictation or a model, single letters which she could name and visualize. Thus, asked if she could imagine the letter "a," she would close her eyes and say, "Yes, I see it. It has a round part and a stroke." Asked to write it, she would draw a line in some direction but was unable to continue. When the examiner drew the letter on the board, she quickly recognized it but could not copy the model. There was also virtually complete inability to draw even the simplest designs either from memory or from a model. Thus, given a square to copy, she drew something resembling a "Z." She also showed severe impairment in estimating the size, distance, location, and spatial relations of objects. In attempting to localize objects in space, there was no tendency to transpose them laterally, that is, no visual allochiria. Also there was no evidence of metamorphopsia.

In short, Badal's patient showed visual disorientation within the setting of intact visual acuity, a condition that was a topic of much clinical investigation and discussion in the 1890's. However, on the basis of further observation, Badal believed that his patient suffered from a spatial disorientation which affected all modalities, by no means being restricted to vision. Thus, while auditory acuity appeared to be intact, she found it difficult to indicate the directional source of sounds. There

were no consistent lateral trends in this regard and thus no evidence of auditory allochiria.

Evidence for a disturbed spatial sense also appeared in the tactual-kinesthetic realm. She could no longer distinguish the right and left sides of her body. "In order to make this discrimination, and even then she sometimes made errors, she had to make the sign of the cross; she knew that she used the right hand for this." Esthesiometric testing indicated slight generalized hypesthesia and a rise in the two-point threshold. But Badal felt that this was not sufficient to explain such "bizarre phenomena" as the following: "It happened frequently that the patient was not able to say which of her fingers had been touched or pricked and, for example, would report the index finger when the ring finger had been pricked . . . . Sometimes the same errors were made even when the eyes were allowed to remain open so that they could guide the tactual impressions; moreover, if one asked Valerie to name the five fingers of the hand, one after the other and in the order in which they were placed, it was rare for her not to commit some error, either in naming them or in classifying them from 1 to 5." Badal believed that these deficits "were due chiefly to a profound alteration of the sense of space" and were not explicable in terms of impaired tactual or kinesthetic sensitivity. There were no disturbances in position sense. "The patient had perfect awareness of the movements which she executed, had a correct idea of the position in which her extremities might be placed and, with her eyes closed, could reproduce this position with the homologous member fairly exactly." Pain and thermal sensitivity appeared to be intact. No areas of cutaneous anesthesia could be discovered.

She also showed a moderate but definite dyscalculia. She could count, do very simple additions, and serial addition by two's was easily accomplished. However, in serial addition by three's, she would invariably fail beyond 24, despite repeated attempts by a variety of methods to combine 24 and 3. Her concept of the basic number series was defective as shown, for example, by her inability to say what number was placed between 14 and 16.

Two further behavioral deficits may be noted. She showed impairment in the execution of a number of skilled acts, including a dyspraxia for dressing. She could not put up her hair without assistance and such familiar skills as knitting or threading a needle were now beyond her capabilities. She was no longer able to dress herself. For example, she put garments on in the wrong order and slipped her arm into the wrong sleeve. She also showed some time disorientation. She could not say confidently what year (1888) it was, but tended to hesitate between 1885 and 1888.

DISCUSSION

Badal considered the question whether the symptoms shown by his patient were organic or functional in nature, but reached no definite conclusion. He did not incline to the view that she was an "hysteric." In describing her premorbid history he stressed that she had never shown any signs of nervous disturbance, and in discussing some aspects of the symptomatology he contrasted them with those shown by hysterical patients. However, it is perhaps worthy of note that Badal described the following characteristics: "The ocular mucosa had not lost any of its sensibility; in contrast, that of the auditory canals and of the nasal chambers was dulled; one could tickle them without eliciting reflexes. There was complete anesthesia of the pharyngeal mucosa, and the finger could be introduced into the back of the throat without eliciting the least reaction. A sudden pressure on the epigastrium, a shock strong enough to give any other person a particularly painful sensation, was easily tolerated."

Looking back at this early case report, it now seems probable that the patient suffered a cerebrovascular insult of rather diffuse nature with significant parieto-occipital involvement as a consequence of the severe eclampsia. As has been mentioned, Badal was inclined to interpret most of the symptoms as expressions of a single basic deficit, namely, a loss of the sense of space.

The fact that Badal described finger agnosia some 70 years ago does not detract from the significant contribution of Josef Gerstmann in "rediscovering" it, so to speak, in describing its relations to other behavioral deficits and, above all, in elucidating its neuropathologic significance. Nevertheless, Badal's report merits consideration not merely for its historic interest, but also because its author's theoretic interpretation still possesses relevance for current thinking about the nature of the Gerstmann syndrome.

Badal's patient showed all the elements of the Gerstmann syndrome—finger agnosia, right-left disorientation, dysgraphia, dyscalculia—and a good deal more, for example, visual disorientation, as manifested in her inability to fixate, locate objects in the environment, and order objects along a visuospatial continuum; constructive apraxia, expressed in an inability to draw and a particular type of dressing dyspraxia; and some degree of temporal disorientation. All of these deficits have been found at times associated with the Gerstmann syndrome. On the other hand, she did not show color agnosia, a symptom that has been mentioned as an "accompaniment" of the Gerstmann syndrome more frequently than has any other.

The clinical picture presented by Badal's patient might be interpreted as a "Gerstmann syndrome," unrecognized as such. However, as it happens, the clinical picture fits equally well the combination of symptoms for which Critchley[8] has suggested the designation of "Leonhard's syndrome,"[11] that is, dysgraphia, dyscalculia, constructive apraxia, and temporal disorientation. Clearly, if the one syndrome was missed, so was the other. Moreover, Badal created his own more comprehensive syndrome of loss of the "sense of space" to account for the observed aggregation of symptoms, a conception which is quite similar to that of later writers, notably Lange.[12]

The situation presented by clinical observation relating to the Gerstmann syndrome since the time of Badal would seem to be about as follows. A relatively large number of behavioral deficits are frequently shown by patients with parietooccipital lesions. A given patient is more likely than not to exhibit a combination of these deficits. Necessarily some patients will show the same combination of deficits, and this circumstance of combination has led to a search for an underlying unitary factor. Moreover, certain combinations of symptoms which have impressed clinical observers have been abstracted and given the special status of "syndromes," for example, Gerstmann and Leonhard. Once these special categories have been established, there is a tendency not only to use them in the observation and description of subsequent case material, but also to allow them to determine to some extent which behavioral events are selected for study and report and which are not.

Obviously, there is nothing inherently wrong about this process of selection and abstraction of symptoms. Indeed, this is a necessary component of the scientific approach to disease. However, it is also obvious that not all syntheses are equally valuable. The "correctness" of any classification is determined only by its meaningfulness. In the case of the Gerstmann syndrome, the cogency in selecting this combination of symptoms would seem to depend upon whether, as a matter of phenomenologic fact, the four deficits do show a distinctively close mutual association, as compared with the degree

of their association with other allegedly "parietal" deficits, and also whether the use of this descriptive category possesses special value for diagnostic inference.

At the present time the meaningfulness of the syndrome in either the phenomenologic or inferential sense remains an open question.[8,13,14] From the phenomenologic standpoint, "incomplete" forms of the Gerstmann syndrome are not rare and more often than not the patient shows other deficits (for example, color agnosia, constructive apraxia, and so on) that have been suggested by one writer or another as properly belonging to the syndrome. Thus it is not known whether the four Gerstmann symptoms show a particularly close association with each other as compared to their "associative bonds" with the other symptoms. Nor is there cogent evidence that the syndrome, considered as a unit, possesses a neuropathologic or psychopathologic significance not furnished by its component elements or by the associated behavioral deficits.

One possible approach to this problem of the combination of symptoms of the "parieto-occipital" type is to make a careful quantitative assessment of the degree of relationship occurring among the several deficits through systematic and relatively unbiased study of an adequate sample of patients. Almost certainly, such an inquiry would show that in general the various deficits are significantly related to one another, thus supporting the tenability of the current hypothesis of a broad "parietooccipital" syndrome. More importantly, the analysis would show whether or not there are significant differences in the degree of relationship of the several deficits and whether specific subgroups of symptoms that are characterized by strong intragroup associative bonds can be isolated. If such clusters of deficits do appear, it could then be determined whether or not they possess particular significance from a neuropathologic, psychopathologic, or general psychologic standpoint. Similarly, it would be possible to determine whether or not they correspond to those syndromes (Gerstmann, Leonhard) that have already been isolated on a more or less impressionistic basis.

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Quantitative Assessment of Motor Function in Cerebral Palsy

Evaluation of Zoxazolamine (Flexin), a New Muscular Relaxant Drug

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IN THE TREATMENT of cerebral palsy, the reduction of spasticity and involuntary movements is an essential preliminary to voluntary muscle control and, by the facilitation of new patterns of useful motor function, a muscular relaxant drug of proven value would be an important aid to therapy and an effective preventive of deformity.

The use of curare, mephenesin, and other muscle relaxants has previously been advocated in therapy but, from a practical standpoint, the results of careful and prolonged trial of these compounds have proved disappointing;[1] in some, the route of administration and the high incidence of toxicity precluded their chronic use, while in others, despite a demonstrable beneficial effect by physiologic studies, a clinical improvement in function was not sustained.

A muscular relaxant compound with ideal properties should be active on oral administration and should decrease involuntary movements and improve the postural stability; it should enhance the range, rapidity, and coordination of voluntary movement without the impairment of muscle strength or untoward effects on vital organs and functions. It was the purpose of the present study, first to determine reliable quantitative methods for the examination of children with motor system disturbances and, subsequently, to apply these test procedures for the objective evaluation of new drugs in the treatment of cerebral palsy.

CLINICAL MATERIAL

Of ten patients included in the study, four had spasticity of the quadriplegic type, two had spasticity of the hemiplegic type, and four had athetosis. Their ages ranged from eight to 18 years, with an average age of 12 years. The sexes were equally represented. Recurrent major seizures in one hemiplegic child were well controlled with diphenylhydantoin (Dilantin) and mephobarbital (Mebaral).

The patients were of average intelli-

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gence, and their ability to perform suitable tests of motor function was the main criterion used in their selection. They were paired as nearly as possible according to age, the clinical type of cerebral palsy, and the severity of motor disability.

QUANTITATIVE TEST METHODS

Measurements of motor function were obtained by objective tests which were modified to suit the performance of each individual patient. In this quantitative examination of the motor system, posture and involuntary movements were studied and estimations of the range, rapidity, strength, and coordination of voluntary movements were obtained.

The postural instability and involuntary movements of patients with choreoathetosis cause shifts in the center of gravity primarily in the transverse plane;[2] a kymographic record of these movements was obtained and the deflections from the base-line were counted during the first two minutes of each record. The cooperation of the patient was essential for the success of this method; in young children with athetosis, a less complicated test gave more constant and reliable results. By a simple test of balance in which the maintenance of an erect head posture was timed, significant changes were observed during treatment with the drug under study.

The maximum range of active abduction in the upper and lower limbs was measured in patients with spastic quadriplegia; the legs were held in extension with braces locked, and exercise skates were worn to facilitate movement. Tests to assess rapidity of movement and muscle relaxation were motivating, yet simple, and a learning factor was not involved; in children whose voluntary movements were grossly retarded and coordination poor, the rate of manipulation was measured by the use of large blocks or pegs, while in those with moderate motor impairment the Minnesota board[3] was employed. Voluntary muscle power was estimated in the upper and lower extremities by the use of weights, and the hand grip was tested with a clinical dynamometer.

Coordination was measured photographically by light-line registration during the performance of the finger-pointing test; cameras were placed at a standard distance from the subject and movements were recorded in frontal and lateral views during a ten-second timed exposure. The maximal range of horizontal and vertical incoordination was measured from photographic prints. In children with minor motor disturbances, shoe-lacing or similar functional tests of coordination were standardized and the performance was timed.

As additional objective tests, specimens of handwriting, straight-line tracings, and short split-frame motion pictures were of some value for the demonstration of changes in motor function, but quantitative assessments of results were not possible.

EVALUATION OF ZOXAZOLAMINE

Zoxazolamine (Flexin), 2-amino-5-chlorobenzoxazole, is a new muscular relaxant drug which, in animal experiments, was found to produce an uncomplicated flaccid paralysis. Compared with mephenesin, Flexin had a much longer duration of action, was more potent, and had a wider margin of safety; its effect was uncomplicated by any preliminary excitement and the incidence of salivation and vomiting was

negligible.[4] The major action of Flexin, as demonstrated by pharmacologic studies, involves depression of polysynaptic pathways in the spinal cord; its neuromuscular blocking effect is weak and unlikely to contribute significantly to the over-all flaccidity.[5] In the present clinical evaluation, Flexin was administered orally as 250 mg. tablets or in suspension; the average initial dose was 250 mg. three times daily and the maximum dose given was 1.5 gm. daily.

In the four patients who were hospitalized for the duration of the trial, the effects of reserpine were also evaluated and compared with those of Flexin. Reserpine facilitates synaptic transmission in the spinal cord[6] and, in the treatment of cerebral palsy, effects opposed to those of Flexin might be expected. However, in some hypertonic infants, a lessening of tense behavior and a return of hyperreflexia toward normal have been reported.[7] In view of the known tranquilizing effect of the drug, its evaluation in the treatment of cerebral palsy seemed warranted. The initial dosage of reserpine was 0.75 mg. daily in three divided doses and, during the four week trial period, the daily dosage was increased gradually to a maximum of 3.0 mg.

Another tranquilizing agent, chlorpromazine (Thorazine), has been advocated for the treatment of cerebral palsy by Basmajian and Szatmari,[8] who observed the abolition of spasticity by electromyographic methods following the rapid intravenous injection of a dose of 50 mg. Also, Denhoff and Holden[9] have reported the beneficial effects of the drug in nine of 18 children with cerebral palsy who were treated with oral doses of 20 mg. three times daily; when assessed by the usual clinical methods, no appreciable specific effect on the muscle status was observed, but irritability and anxiety were less evident. The muscular relaxant effects of chlorpromazine, in an oral dose of 25 mg. daily, were investigated by the objective clinical methods described in one patient with spastic quadriplegia in the present study; at the beginning of the Flexin trial the patient had vomited and complained of dizziness, and chlorpromazine was substituted.

CONTROLS

A fundamental criterion of a valid pharmacologic experiment is that the phenomena observed are the result of the effects of the drug and not of extraneous factors. During the quantitative motor evaluations of the patients in this study, tests were applied by the same examiners and environmental influences such as the test situation, the time of day, and the interval between test days were kept constant. Four patients were hospitalized in the same environment, while six attended as out-patients; the results of the trial therapy were assessed separately in the two groups.

The beneficial effect of physical habilitation and the marked improvement in results with practice were differentiated from the specific effects of the drug by the use of simultaneous controls and control periods. The patients, paired as nearly as possible according to age, the clinical type, and the severity of the cerebral palsy, were treated equally with regard to physical and other forms of traditional therapy; they were allocated at random to the trial or control group so that, apart from the drug treatment under study, there was no systematic difference in the factors which might influence the test results. Psychologic

effects of the new treatment were controlled by the use of a placebo, and the double-blind technic was employed in order to avoid bias in both the allocation of patients and the assessment of results. The test drug and placebo were administered to each patient alternately for one-month periods and, in addition to the comparison of results in simultaneous controls, each patient served as his own control.

The majority of the tests for the assessment of motor function were performed twice weekly for an average period of five months by the patients admitted to the ward; three readings were obtained on each day of testing. The out-patient trial was continued for three months and tests were performed at intervals of one or two weeks.

At the beginning of the trial and at monthly intervals thereafter, the degree of motor impairment and the progress of each patient were assessed by the physician and the physical, occupational, and speech therapists. Some measurements of voluntary muscle power and range of movement were obtained in addition to a subjective appraisal of function, and a speech recording was made at each examination.

RESULTS

The objective test results obtained during treatment with the trial drug were compared with those of the placebo periods; the means and variances of the readings were calculated, and differences as a result of the action of the drug were analyzed statistically and assessed at the 5 per cent level of significance. In tables 1 and 2 the differences between trial and placebo test results are expressed in terms of significance, and

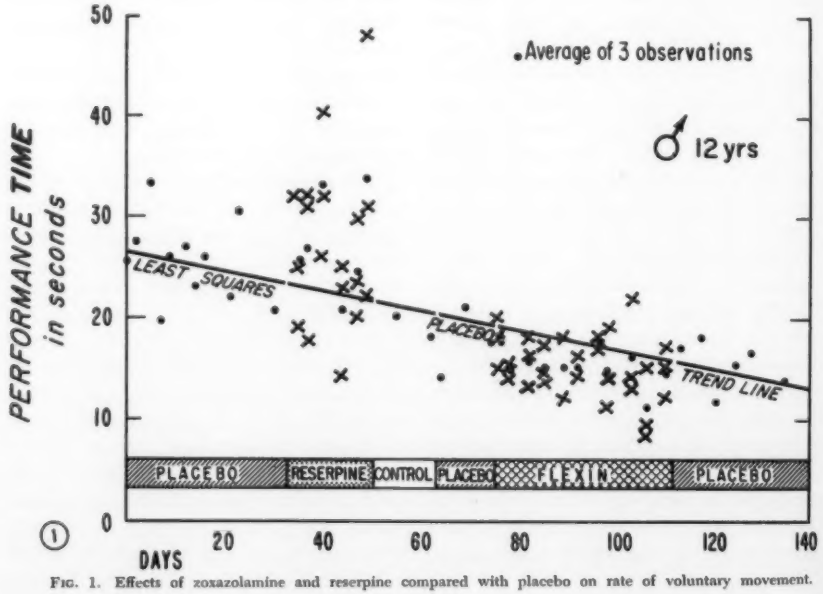

FIG. 1. Effects of zoxazolamine and reserpine compared with placebo on rate of voluntary movement.

TABLE 1
EFFECTS OF ZOXAZOLAMINE COMPARED WITH RESERPINE IN FOUR CHILDREN WITH CEREBRAL PALSY

Motor System Evaluation	Zoxazolamine: Spastic C.P. Patients 1	2	Zoxazolamine: Athetoid C.P. Patients 3	4	Reserpine: Spastic C.P. Patients 1	2	Reserpine: Athetoid C.P. Patients 3	4
By Objective Tests:								
Posture and involuntary movement			XX	XX			O	O
Range of voluntary movement	XX	XX			O	O		
Motor coordination	XX	X	XX	XX	– –	–	–	
Rate of movement	XX	X	X		– –	–	– –	
Muscle strength	O	O			O	O		
By Subjective Tests:								
Functional ability	X	X	X	X	O	O	–	–
Spasticity	X	X			O	O		
Hypertonia and involuntary movement			X	X			X	O
Range of voluntary movement	X	X			O	O		
Muscle strength		–				–		
Speech			X	X			O	O

XX, significantly improved (P=.05); X, improved; O, no change; –, worse; – –, significantly worse (P=.05).

in figures 1 to 4 the magnitude of these changes and the means and variances of the readings are illustrated in test examples.

An improvement trend in test results, which occurred with practice and which to some extent was due to therapies other than the drug, was observed by comparing the test values in the simultaneous control patients. The magnitude of the practice factor in the individual patient could be established by a least squares line fitted from the test results obtained during treatment with the placebo. The performance values recorded during the trial medication periods were compared with the placebo trend line and differences were analyzed statistically.

Figure 1 illustrates the method of assessment of the effects of practice on the test performance and the exclusion of this factor in the evaluation of the drug under trial. The subject is a boy, aged 12 years, with spastic quadriplegia and minor athetoid movements, and his performance time in a test of coordination and rapidity of movement is recorded at intervals of two to three days and compared during treatment with placebo, reserpine, and Flexin. The average value of three observations at each test day is plotted for the placebo periods, and the practice trend-line is fitted by the least squares method. The values obtained during treatment with reserpine and Flexin, and recorded individually and as the mean of three observations, are significantly different from the placebo trend-line. With reserpine the rate of performance and motor coordination are decreased ($P=0.03$), whereas during treatment with Flexin the rate is increased and the coordination improved ($P=0.001$).

In table 1 the effects of Flexin are compared with reserpine in the treatment of four children with cerebral palsy who were hospitalized for the study. Two had spastic quadriplegia and two had severe athetoid movements and hypertonia which affected all limbs. The

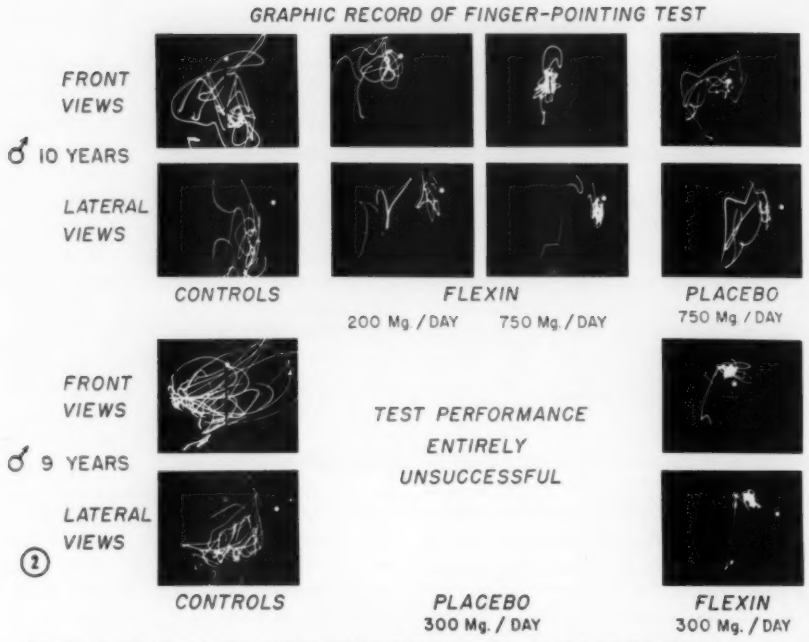

FIG. 2. Effect of zoxazolamine (Flexin) on incoordinated movements of children with athetosis.

average age of the patients was ten years; those with spasticity walked with the aid of crutches, while the athetoid children were nonambulant. The motor system evaluations, obtained by the objective methods described above and by the subjective appraisals of physician and therapists, show improvement without significant loss of muscle power during treatment with Flexin, whereas either impairment or little or no beneficial change in motor function is apparent during treatment with reserpine.

In both patients with athetosis, tests of head posture and motor coordination showed significant improvement during treatment with Flexin and speech was slightly more intelligible. Figures 2 and 3 show the degree of incoordination of these children by photographic light-line registration and the finger-pointing test. In the initial control records the maximal range of horizontal and vertical movement, measured from the prints of frontal and lateral views and expressed as the mean of three observations, is charted as 100 per cent range of incoordination. One child received Flexin for one month, followed by treatment with a placebo for a similar period, while the other served as a simultaneous control. With Flexin the improvement in coordination shows some relation to the dose, and with 750 mg. daily the decrease in range of movement is significant when compared with the initial control. That practice is an unlikely factor in this improvement is apparent from the com-

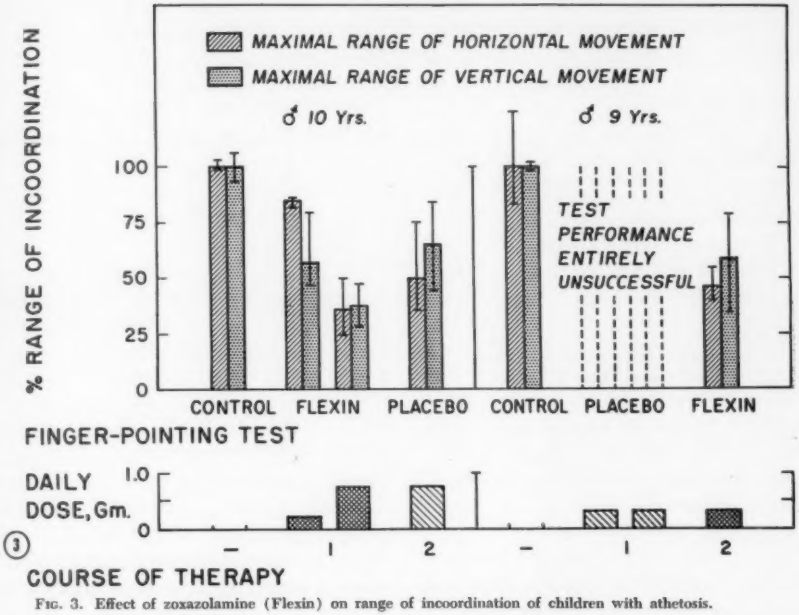

FIG. 3. Effect of zoxazolamine (Flexin) on range of incoordination of children with athetosis.

parison with the performance of the control patient; in this boy the tests repeated during placebo treatment were entirely unsuccessful and graphic records could not be obtained. Following withdrawal of Flexin in one patient, the improvement in coordination was not maintained.

Of six patients who were not hospitalized for the drug trial, two had spastic quadriplegia, two had hemiplegia, and in two athetoid movements and hypertonia were the principal neurologic signs. Table 2 shows the changes observed in the motor system examination of these patients during treatment with Flexin; the degree of change was established by a comparison of the quantitative assessments of motor function during treatment with placebo and Flexin. The test results in the athetoid patients showed a significant degree of improvement; no changes were observed in those with hemiplegia, and in one patient with spastic quadriplegia, some increase in rapidity of movement and coordination occurred but the degree of change was not significant.

The effective daily dose of Flexin varied between 0.6 and 1.5 gm., or 0.02 to 0.05 gm./kg. body weight; the mean effective dose was 0.03 gm./kg. daily.

In the patient with spastic quadriplegia who received chlorpromazine, the rate of voluntary movement and motor coordination were significantly decreased and the functional ability impaired (figure 4). However, by subjective tests, spasticity and the tendency to clonus were diminished and the range of movement was increased; the patient showed less anxiety in the test situation

TABLE 2

EFFECTS OF ZOXAZOLAMINE IN SIX PATIENTS WITH CEREBRAL PALSY

Motor System Evaluation	*Cerebral Palsy Patients*					
	Spastic Quadriplegia		*Spastic Hemiplegia*		*Athetosis*	
	1	*2*	*3*	*4*	*5*	*6*
By Objective Tests:						
Posture and involuntary movement					XX	
Range of voluntary movement	O				XX	
Motor coordination	X		O	O	XX	XX
Rate of movement	X		O	O	XX	XX
Muscle strength			O	O		
By Subjective Tests:						
Functional ability	X		O	X	X	X
Spasticity			O			
Hypertonia and involuntary movement					X	X
Range of voluntary movement	X		O	O	O	
Muscle strength	O			O	–	O
Speech	X					O

Side effects necessitated drug withdrawal

XX, significantly improved (P=.05); X, improved; O, no change; –, worse.

and the power of her grip was significantly enhanced.

SIDE EFFECTS

During treatment with Flexin side effects were encountered in five of the ten patients in the trial, and in four patients the drug was withdrawn. Nausea and vomiting occurred in three patients and dizziness in two; a urticarial skin rash with angioneurotic edema, which developed in one child at the beginning of a second course of Flexin, was probably a reaction to the drug but the causal relation was not proved. In one hemiplegic girl the incidence of seizures was

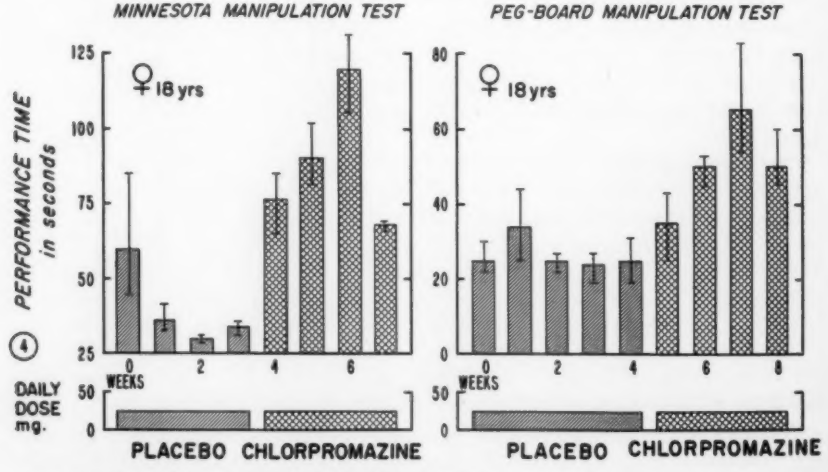

FIG. 4. Effect of chlorpromazine on rate of voluntary movement.

increased, and in a boy with hemiplegia transient twitching in the deltoid muscle was reported. The vital capacity, measured in eight patients, was increased in two patients with athetosis, reduced in two with spastic quadriplegia, and unchanged in the remainder; the changes were not significant, however, at the 5 per cent level of probability. Apart from two patients who showed some loss of power in hip flexion with a dose of 1.5 gm. daily, impairment of muscle strength was not observed.

A relation between dosage and toxicity was not established, but in two patients vomiting or skin rash became troublesome only when therapy was reinstituted after a control period. In patients with athetosis, drooling was less evident and toxic effects did not occur. In all patients, examinations of the blood and urine were performed at monthly intervals throughout the trial and no abnormalities were detected.

COMMENT

Before valid conclusions can be drawn regarding the therapeutic efficacy of a new drug, adequate and precise methods for the accurate and objective measurements of its actions must be established.

Though the potential value of muscular relaxant drugs in the treatment of cerebral palsy may be demonstrated by electromyographic studies, from a practical therapeutic standpoint the assessment of effects on motor function is of greater importance in the clinical evaluation of such compounds. In a critical report concerning the effects of neostigmine in patients with cerebral palsy, Perlstein and Barnett[10] have referred to the lack of concordance of evidence from physiologic and clinical studies, and, in the demonstration of progress during treatment of athetosis by re-educational methods, Phelps[11] has advocated the measurement of functional ability by tests of performance.

In the present investigation, the objective tests employed and the experimental design were adequate to allow statistical analysis of results and a valid evaluation of the therapy under study. The demonstration of a dose-response relation, the axiom of a true drug effect, was attempted (figure 3), and the results of treatment with the drug under trial were compared with those of a compound with opposite effect (figure 1). By these methods and by the exclusion of the effect of practice, small but significant changes in objective test results could be ascribed to the effects of the drug.

In the patients who were hospitalized and tested twice weekly, the incidence of significant differences between trial and placebo results was higher than in out-patients who were tested less frequently. In two patients with spastic hemiplegia who attended at intervals of two weeks, few readings were obtained and changes as a result of the drug were not observed. Improvement in motor function during treatment with Flexin showed some relation to the type of cerebral palsy; in patients with athetosis and without muscle weakness, the efficacy of the drug seemed greater than in those with spastic paralysis.

The value of Flexin in a limited number of patients and in certain types of cerebral palsy has been demonstrated in this preliminary investigation. A further prolonged trial is recommended, particularly in young children, so that the efficacy of the drug as an aid to physical habilitation may be observed on a long-term basis.

In accordance with the results of electromyographic studies previously reported,[8] a reduction of spasticity and relief of clonus were observed during treatment of one patient with chlorpromazine. However, in the present investigation, both chlorpromazine and reserpine caused impairment of functional ability. As aids to the physical habilitation of cerebral palsy patients, the limited value of these drugs is suggested.

SUMMARY

Objective tests have been determined for the quantitative assessment of motor function in ten children with cerebral palsy, and their value has been demonstrated in the controlled evaluation of muscular relaxant drugs.

By a suitable experimental design, extraneous factors which might influence the test results have been controlled; a method has been described for the assessment of improvement in performance due to practice and for the exclusion of this factor in evaluation of treatment.

Of ten patients who received zoxazolamine (Flexin) for a one-month period, small but significant improvements in tests of motor function were observed in six patients and some degree of improvement was apparent in one. The efficacy of the drug seemed greater in patients with athetosis and without muscle weakness than in those with spastic paralysis. In four patients toxic effects necessitated the withdrawal of the drug; vomiting was the most troublesome symptom.

In a limited trial of reserpine in four patients and chlorpromazine in one, the rate of voluntary movement was retarded and functional ability was impaired.

Flexin was kindly supplied by McNeil Laboratories.
The authors wish to thank the staff of the rehabilitation department for their assistance.
We are indebted to Dr. Winthrop M. Phelps for permitting the inclusion of his patients, and to Dr. Seymour Geisser for the statistical analyses.

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ADDENDUM

Since the completion of the present report, the clinical use of zoxazolamine has been described in four articles (J.A.M.A. 160:742, 745, 749, and 752, 1956).

On Neurologic Terminology, Eponyms and the Lasègue Sign

Robert Wartenberg, M.D.

IT IS HIGH TIME that neurologists do some thorough cleaning in their own backyard of terms and eponyms they use every day. Many of these are indubitably obsolete, confusing, inadequate, or just plain wrong.

To start with, the general term "neuropsychiatry" is a bastard word and misnomer. We say "neurophysiology" and "neurosurgery," which are correct contractions of "neurologic physiology" and "neurologic surgery." "Neuropsychiatry" is not a contraction of this kind, because there is no such thing as neurologic psychiatry. We contract "otology and rhinology" into "otorhinology." "Neuropsychiatry" cannot be regarded as a contraction of this kind, because the ending of the two words is different. We do not say "ophthalmosurgery" to abbreviate "ophthalmology and surgery."

"Pseudobulbar palsy" is a wrong term. There is nothing "pseudo" about this palsy. It is fearfully real. It is only spastic rather than flaccid. We do not call spastic spinal paralysis "pseudospinal paralysis" just because it is not flaccid. The correct term should be "supranuclear bulbar palsy" or "spastic bulbar palsy."

In the same way, "myasthenia gravis pseudoparalytica" is not a correct term. No myasthenic patient would agree that he has a pseudoparalysis. It is, unfortunately, a very real one, only not of the kind that we see in anterior horn diseases.

"Facial hemiatrophy" is a not quite accurate term. The atrophy is not "hemi," but sometimes very pronounced. "Hemi" should be related to the face and not to the atrophy. Therefore the term "hemifacial atrophy" is by far more exact.

When the patient has spontaneous abnormal sensations in the skin, we call them "paresthesias." This is not correct. The term "paresthesia" implies external stimulation. "Para" means "beside." If somebody has abnormal sensations when his skin is touched, he has something beside or instead of the normal sensation. These are real paresthesias. If the sensations occur without external stimulus, the broader term "dysesthesia" should be used.

In atlases of anatomy and in textbooks, the term "nervus cutaneous antibrachii" is used. This is not correct. It is "ante," not "antibrachii." It is "before" the arm, and not "against" it.

"Parkinsonism" is an ugly term. "Parkinson" is clear enough, particularly when used with an adjective, as idiopathic, postencephalitic, sclerotic, and so on. An "ism" is a tenet, an addiction, a doctrine and, properly, should not be used to

designate a variety of disease.

For the term "Rombergism," newly used by some, there is only one classification – horror linguisticus! How about Babinskiism, Lasègueism, and so on?

Reflexes should be designated as such. There is no reason to call them, interchangeably, jerks or kicks. Physiology knows reflexes but not jerks or kicks. It is a mystery why, in a textbook of 1955, there are, on the same page, the titles: "Biceps Reflex" and then "Triceps Jerk."

It would be most helpful didactically if neurologists would agree to term reflexes according to the muscle involved. A lot of confusion extant could be thus avoided. Therefore, there should be "orbicularis oculi reflex," "triceps reflex," "biceps reflex," "brachioradial reflex," "finger flexor reflex," "quadriceps reflex," "triceps surae reflex," and "plantar muscle reflex."

There is a brachioradial reflex. This term is unequivocal and says everything. But still a textbook appearing in 1955 uses instead "Radialis Periosteal Reflex (Supinator Jerk)." This term is full of mistakes. "Radialis" is wrong, if it means "pertaining to the radius." This is not a radius reflex. "Radialis" is wrong if it pertains to the muscle involved, whose name is "brachioradialis." It is not a "periosteal reflex," since it has nothing to do with the periosteum. The muscle is not a supinator, and the whole is not a jerk, but a reflex.

Most textbooks still speak of abdominal reflex and mean the superficial abdominal reflex. It is, however, highly important to distinguish between the superficial and deep abdominal reflexes. The diagnostic value of their dissociation (superficial reflexes lost, deep reflexes exaggerated) is of the greatest practical importance.

Eponyms serve a useful purpose. They are short, stick easily in the mind, serve as a good mnemonic prop, and pay honor to whom honor is due. They relieve us of the necessity to compress into one or two words the essential features of a complicated phenomenon, be it a disease or a reflex. Students like to use eponyms, since an eponym for them is a *signum eruditionis*.

Still, it is better to use a clinical, pathologic, descriptive term which tells the student something about the nature of the phenomenon, which an eponym does not. "Infectious chorea" is better than Sydenham's chorea." Hardly any student will remember the name Sydenham from having read his original Latin treatise on chorea written in 1686. "Neurofibromatosis universalis" is better than "von Recklinghausen's disease," all the more so since another disease is named for him: generalized osteitis fibrosa. Hemochromatosis, too, carries his name. What, then, is meant when we say von Recklinghausen's disease?

"Spastic spinal paralysis" says a great deal more than "Erb's," "Charcot's," or "Erb-Charcot's" disease. These two names have been eponymically connected with many other diseases. "Pseudotabetic pupillotonia" is better than "Adie's syndrome." "Ophthalmoplegic migraine" tells more than "Möbius' disease." Popular as the eponym Brown-Séquard is, we instruct the student more when, in summary, we say "This is a case of hemisection of the spinal cord," rather than "This is a case of Brown-Séquard's paralysis."

"Hemiplegia alternans facialis" is better than "Gubler's syndrome," "hemiplegia alternans hypoglossica" is better than "Jackson's syndrome," and "tuberculous

spondylitis" is better than "Pott's disease." If we summarize a case to the students as "upper brachial plexus palsy" or "lower brachial plexus palsy," we tell them more than if we say "Erb-Duchenne" or "Dejerine-Klumpke" disease.

This list could be enlarged indefinitely. It shows clearly the advantages of a term which refers to the nature and content of a medical phenomenon, rather than to the man who allegedly first described it.

On final critical analysis, an eponym says nothing, is apt only to confuse the issue, or is at least superfluous. As a young student, I studied diligently the different forms, divisions, and subdivisions of muscular dystrophy, with their single or double eponyms. This was then, for me, the alpha and omega of knowledge and the height of erudition. I no longer think so, and now I tell my students to forget all about proper names of the dystrophies.

The plethora of proper names for reflexes has led so far as to require numbers for some eponyms, since some investigators have described more than one reflex. And so we find Babinski 1, 2; Bechterew 1, 2; Bing 1, 2. Even Wilson speaks of Babinski's second sign. Unfortunately, other writers understand something different by this: not unilateral leg raising in hemiplegia, but the toe fanning sign.

Nothing, of course, can be said against eponyms *per se*. It is their inflation, their over-use, the eponymania, endemic particularly in middle Europe, against which a strong voice should be raised.

Two Hungarian authors,[1] describing the reflexes in their case, use 11 eponyms, including the name of one of the authors. They say: "Benedek bilaterally negative." Having studied reflexes for many years, I have never come across the reflex of this author, nor have I been able, thus far, to find out what is meant by this reflex.

The main trouble with eponyms is that they are often obviously incorrect. Even with the history of the phenomenon in full view, it is often impossible to say after whom the phenomenon should rightfully be named. In only a few cases is it possible to trace a disease, a sign, a reflex definitely to a certain author. In most cases there is a wide choice. We may consider who first described it, recognized its significance, definitely outlined it, introduced it, gave a correct explanation, gave it a name. If a disease, for instance, is named according to the author who first intimated its existence, the description may have undergone so many changes over the years that it now appears to be a vastly different disease.

The selection of a name for an eponym is often arbitrary, influenced by national, local, or purely personal "special interests." Prejudice plays its part and often plain ignorance. The yearning for eponyms and the desire to please everybody have led to such horrors as found in the following titles of articles appearing in 1955: "Sturge-Kalischer-Weber-Dimitri-Krabbe disease," and "Laurence-Moon-Biedl-Bardet syndrome."

In allotting eponyms, a previous description of the particular phenomenon is often overlooked. Hardly anyone will believe that Babinski's sign was described before Babinski, and still it was done by the German, E. Remak, in 1893 and by the Englishman, Marshall Hall, in 1841, 55 years before Babinski. For exophthalmic goiter, the Germans never use any eponym except Basedow, although the Irishman, Graves, described

this disease five years before Basedow. We always speak of adiposogenital dystrophy as Fröhlich's disease, whereas Babinski described it one year earlier. To be correct, it should not be Tinel's sign, but Hoffmann's sign, because the physiologist Paul Hoffmann described it before Tinel. The lumbar puncture which carries the name of Quincke was done first, not by him in 1891, but by the New Yorker, Corning, in 1889. Dagnini described slowing of the pulse following pressure on the eyeball before Aschner. Adie's syndrome, association of pupillotonia with loss of reflexes, was described by the Frenchmen, Weill and Reys, five years before Adie. The Germans use the eponym Simons for progressive lipodystrophy. However, the Spaniard, Barraquer-Roviralta, described this condition five years earlier. What is called Foster Kennedy syndrome, retrobulbar neuritis on the side of a frontal lobe tumor with papilledema on the contralateral side, was described before Kennedy by Paton. This author, however, is seldom given credit for this syndrome.

It is axiomatic that the eponym Bernhardt-Roth (1905) is correct for neuritis of the lateral cutaneous nerve of the thigh. Nobody has ever used any other eponym. And still it is a fact that this condition had been described before by Hager in 1895, Remak 1881, Bernhardt 1878, Nothnagel 1872, Krafft-Ebing 1871, and by Bäumler in 1867. This is not rumor or gossip: I have the corresponding articles before me. Bäumler, in his article of 1867, reported on a patient convalescing from typhoid fever who had a complete anesthesia of the skin on the right side in the area of nervus cutaneus femoris medius and anterior externus. Nothnagel, in 1872, found in a patient convalescing from typhoid fever "a sharply circumscribed zone of diminished sensibility to touch and temperature on the outer frontal aspect of the left thigh" as the only anomaly in the nervous system.

A volume could be compiled to enumerate such instances where a rational doubt can arise whether some eponym is correctly applied. The confusion rampant here is illustrated by the following example. There is a "hard palate reflex" consisting of protrusion of the lips on stimulating the hard palate. This is called by some "Henneberg reflex," by some "Laehr-Henneberg reflex." Oppenheim, in his textbook, refers to an article by Laehr and Henneberg on this reflex. Nobody seems to know whether this is the same reflex or two different reflexes, and who described it first – Laehr or Henneberg, or both together. The fact of the matter is that the reference of Oppenheim is wrong. There is no article by Laehr and Henneberg. There is only the article by Henneberg in which he mentions that Laehr drew his attention to this reflex.

A striking example is the confusion in and around eponyms in the story of Lasègue's sign. It is basically a tragic story, but not without a touch of humor. The sign is elicited as follows: The patient, lying supine, keeps his leg straight at the knee joint and raises his leg. When he then has pain in the back of the leg, it is said that the "straight-leg-raising sign" is positive. This occurs in sciatica. The sign is known as Lasègue's sign. The test has, since Lasègue's time, gone through so many modifications that it is better to speak of "pain-on-stretching test." Next to the Babinski and Romberg signs, it is one of the most popular signs in neurology.

The physician, psychiatrist, neurologist, epidemiologist, "the universal specialist," Ernest Charles Lasègue (1816-1883), published in 1864 in Archives Générales de Médecine an article entitled: "Considérations sur la Sciatique." It has become a classic. It was quite natural that everybody should assume right away and without question that Lasègue described here his famous sign. And, indeed, in leading textbooks of neurology like Oppenheim (even in the seventh edition of 1923), Wilson (even in the second edition of 1955), in Handbooks of Neurology (Lewandowski, 1910-11; Jung, 1953), Medical Encyclopedia (Kelly, 1948), monograph on sciatica (Lewin, 1943), in all these works and in many others consulted, there is invariably the statement that Lasègue described his sign in 1864 and often also a reference to his article in Archives Générales de Médecine. In numerous monographs on sciatica, there is the statement: "Lasègue showed in 1864 . . . " However, it is an indisputable fact that this famous article of Lasègue of 1864 contains nothing, absolutely nothing about this sign, not even a hint.[2] It is highly embarrassing to state the plain fact that all those authors mentioned who quoted Lasègue's article of 1864 as a source of Lasègue's sign did not read the article. And this applies to such men as Oppenheim and Wilson.

It is still more embarrassing to point out that Oppenheim quoted, also in connection with Lasègue's sign, an article of de Beurmann.[3] Oppenheim evidently did not read this article either, because de Beurmann says there: "Lasègue always looked for this sign and never failed to emphasize its value. We believe it was he who discovered it first, though he did not mention it in his article published in the Archives de Mèdecine in 1864 . . . " Lasègue, until his very death in 1883, never published a word about this sign. The first description of Lasègue's sign was given in 1881 in Paris, in a doctor's thesis by Forst,[4] a pupil of Lasègue. Forst mentioned that it was his teacher Lasègue who had first drawn his attention to this sign.

Forst's thesis appeared in 1881. As D. T. Dimitrijevic[5] has shown, there appeared one year earlier in a Serbian journal an article of the Belgrade physician and story teller, Lazar K. Lazarevic[6] entitled: Ischias postica Cotunnii. Here a complete description of the straight-leg-raising sign is given. Later, in 1884, Lazarevic gave a more complete description of the straight-leg-raising sign in German.[7] According to Dimitrijevic, the German article of 1884 is more detailed than the Serbian of 1880, but the latter contains all the essential points of the former.

Lazarevic not only described the straight-leg-raising sign before Forst, he was also the first to give the correct explanation for this sign, that is, that the pain elicited is due to stretching of the nerve. Forst explained the pain evoked as due to pressure of the posterior muscles of the thigh on the trunk of the sciatic nerve. Forst said that this was the opinion of Lasègue. The thesis was dedicated to Lasègue, who was its sponsor. Lasègue approved the thesis and did not criticize the views expressed therein.

In the above-mentioned article of 1884, de Beurmann criticized the view of Forst and emphasized that the pain on raising of the straight leg was due to stretching of the nerve. He supported his view by experiments on a cadaver. He exposed the trunk of the sciatic nerve

on the posterior aspect of the thigh between the biceps and the semitendinosus. A part of the nerve was resected and replaced by a rubber tube of the same length. He could observe that, on performing the Lasègue test, the length of the rubber tube increased from 10 to 18 cm. by maximal flexion of the straight leg toward the pelvis.

Although Lazarevic in 1880 not only gave the first description of the straight-leg-raising sign but offered the correct explanation, his work went completely unnoticed. I have never met any reference to this article of Lazarevic. In the largest existing biographic medical encyclopedia,[8] there are five lines about Lazarevic, but neither of these two articles of his on sciatica is mentioned. There was no obituary on Lazarevic in any non-Serbian journal, nor in the Viennese Medical Journal which published his article in 1880. Sic transit gloria mundi!

It is best to call this sign the straight-leg-raising sign, and if an eponym is applied at all, it should be Lazarevic or Lazarevic-Lasègue.

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■ Even in cases of epilepsy due to a disease of the encephalon, the cause of the fits may originate from some points of the skin, and the prevention of the passage of the aura, in such cases, can prevent the fits. There are four cases of this kind that I know, in three of which the disease consisted in a tumor in the brain. In my animals the same thing exists; although the alteration of the spinal cord – which is the cause of epilepsy – persists, the aura being interrupted by the section of the nerves which go to the skin of the neck and face, epilepsy so far as I have been able to ascertain, ceases. The aura may originate from any part of any centripetal nerve, and there is no doubt that its place varies according to the location of disease in the nervous centres, when it is due to such a disease.

C. E. Brown-Séquard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

Changes in the Glycoproteins of the Cerebrospinal Fluid in Neurologic Diseases

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THE PROTEIN-BOUND CARBOHYDRATES of the blood, called also glycoproteins,[1] have been reported to be greatly increased in several pathologic conditions.[2–4] The blood polysaccharides in brain tumors have been investigated recently in our laboratory[5] and significant increases were found in malignancy. It may be assumed that the pathologic changes due to diseases of the central nervous system are reflected to a greater extent by the spinal fluid than by the blood. Therefore, our investigations were extended to the protein-bound carbohydrates of the spinal fluid. Methods for the determination of the various forms of bound carbohydrates in the spinal fluid have been worked out recently.[6] This paper describes the application of these procedures to the fluids of patients with various types of neurologic disorders.

MATERIALS

The cerebrospinal fluids from 150 patients were collected. These were obtained by lumbar puncture and in a few instances by pneumoencephalography. The fluids were free from blood, and if turbid they were centrifuged until clear. Fluids were taken from 129 neurologic patients with such disorders as multiple sclerosis, neurosyphilis, neoplasia, epilepsy, cerebral thrombosis, infectious polyneuritis, and other miscellaneous neurologic diseases. Fifteen of the remaining 21 fluids were from patients with non-neurologic disorders and were used as controls. The other six fluids were from pregnant women. Since the blood polysaccharides increase in this condition,[7] these fluids were handled separately from the control group.

Spinal fluids from healthy persons were not obtainable. Therefore, for purposes of comparison, we used fluids from patients undergoing surgery for non-neurologic conditions under spinal anesthesia. All patients were in good nutritional state, free from any systemic disease known to affect the nervous system, and free from any disease or condition

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known to cause elevation of the serum glycoproteins such as malignancy or infection.

METHODS

"Total polysaccharide," alternately called bound carbohydrate or glycoprotein, refers to carbohydrates associated with the protein. In the strict sense, polysaccharides are compounds that yield only simple carbohydrates on hydrolysis. No evidence has as yet been obtained for their presence in the spinal fluid, although a polysaccharide has been isolated in small quantity from serum.[8] The method applied here requires alcohol precipitation of all the high molecular weight carbohydrates, whether in the free form or bound to the proteins. The total polysaccharides were determined as hexoses. The method has been described in detail by Roboz and co-workers.[6]

"Gamma polysaccharides" are the carbohydrates bound to the gamma globulin. The gamma globulin is separated from the rest of the proteins by precipitation.[9] The precipitate is washed twice with 80 per cent ethanol to remove traces of the free sugars, dissolved in 1 ml. of 1.25 per cent of sodium carbonate, and the solution is further treated as described.[6]

The total protein was measured by a modification of the biuret method of Weichselbaum.[10] Using the recommended ratio of one volume of solution to one volume of reagent frequently resulted in a turbid solution. Since turbidity produces higher readings in the colorimeter, the ratio was changed to 1.5 volumes of fluid to 3.5 volumes of reagent. This change of the ratio eliminated turbidity.

The gamma globulin was determined according to Roboz and co-workers.[9] When only a small volume of fluid was available, the precipitated gamma globulin was dissolved in only 2 ml. of 1.25 per cent sodium carbonate and determined directly as described.

In the presentation of the results, the significance of variations of the average values from the control was calculated using the standard "t" test of significance.

RESULTS

Total Polysaccharide and Total Protein Content of the Spinal Fluid

The average values for the total polysaccharide and total protein content and ratios in the spinal fluids of the controls and patients with multiple sclerosis, neurosyphilis, brain tumors, epilepsy, cerebral thrombosis, and infectious polyneuritis are shown in tables 1 and 2 and in figures 1, 2, 3, and 4.

The average total polysaccharide and its ratio to the total protein in the control show small deviations from the means.

Multiple sclerosis. The diagnosis of this disease was based on the criteria suggested by Schumacher.[11] All patients had clinical evidence of scattered and discrete lesions of the nervous system, with histories of exacerbation and remission of the neurologic manifestations. The spinal fluids from 25 patients were studied for their polysaccharide and total protein content. Sixteen were in clinical exacerbation and nine were in remission. All were free from any serious disease of any of the other organ systems. The results in table 1 show that the average total polysaccharide is moderately increased over the controls. The ratio, however, is significantly increased over that of the control. Statistical comparison of the ratios in the groups in

TABLE 1

TOTAL POLYSACCHARIDE AND TOTAL PROTEIN IN CEREBROSPINAL FLUID

Disease	*No. of Cases*	*Average Total Polysaccharide mg./L.*	*Average Total Protein mg./L.*
Control	15	14.4 ± 4.0	526 ± 118
Multiple sclerosis	25	18.5 ± 5.6	484 ± 182
Neurosyphilis	24	22.2 ± 6.9	539 ± 136
Brain tumors	16	42.8 ± 51.5	853 ± 671
Cerebral thrombosis	6	23.7 ± 13.2	504 ± 244
Infectious neuritis	5	28.8 ± 11.1	1,337 ± 436
Idiopathic epilepsy	10	13.1 ± 3.7	423 ± 163
Symptomatic epilepsy	8	18.2 ± 7.5	452 ± 171

exacerbation and remission did not show any significant difference.

Neoplasms of the central nervous system. The histologic type of the growth was established in ten of the 16 patients studied at operation or autopsy. Nine of the ten had primary neoplasms, six of these cases had astrocytomas, and the remaining three had ependymoblastoma, acoustic neuroma, and hamartoma, respectively. The tenth patient had metastatic bronchogenic carcinoma.

The remaining six cases were diagnosed clinically as neoplasms of the central nervous system. Three had primary malignant growths elsewhere, with manifestations of metastasis to the central nervous system. The other three probably had primary tumors.

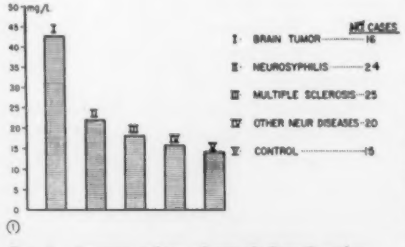

FIG. 1. Average values of protein-bound carbohydrates in various neurologic diseases.

The average values of protein-bound carbohydrates of the cerebrospinal fluid in the proved and clinically diagnosed tumors are shown graphically in comparison with the control in figure 2. The values are elevated in both tumor groups. The results show that the proved tumors have the highest total polysaccharide content. Figure 3 compares the ratios in cases of brain tumors with the controls. All the ratios are significantly elevated, with the greatest increase in the group of proved tumors.

No direct correlation could be found between the histologic type of tumor and the values of the total polysaccharide and its ratio to the total protein. Although the highest ratios are associated with the greatest increases of the total proteins, it is significant that in some cases, even with normal protein contents, the ratios are elevated.

Table 1 and figure 1 present the average total polysaccharide in brain tumors as compared with other neurologic diseases. It can be seen that the greatest increase is found in brain tumors. Although there are wide deviations of individual values of the total polysaccharide and the total protein from the means, table 2 and figure 4 show that the

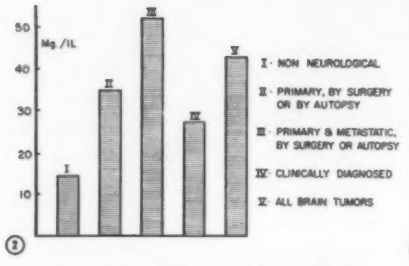

FIG. 2. Average values of protein-bound carbohydrates in different types of brain tumors.

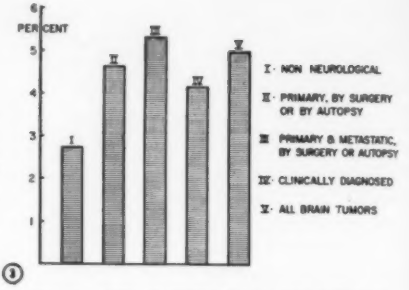

FIG. 3. Ratio of protein-bound carbohydrate to protein in brain tumor.

highest ratios are found in brain tumors as compared with other neurologic diseases.

Cerebral thrombosis. The underlying vascular disease in the six cases studied was arteriosclerosis; one patient also had hypertension and another diabetes mellitus. Four patients presented the syndrome of middle cerebral artery occlusion. One patient had vertebral and basilar artery thrombosis, and another had a posterior cerebral artery occlusion. All spinal fluids were free from blood and had been obtained within 72 hours of the onset of the occlusive episode.

The average total polysaccharide in the spinal fluid in this condition is moderately increased over the control and shows fairly wide variations from the mean. The average total protein does not differ markedly from the control, but the ratio is significantly increased.

Infectious polyneuritis. All five cases studied had classical manifestations of the disease, with bilateral and symmetric weakness of all extremities and greatly diminished to absent deep tendon reflexes. Three patients had stocking-and-glove type of sensory loss. The spinal fluids had normal cell counts and the total protein values averaged $1,337 \pm 436$ mg./L. This is very high compared with the control value of 526 ± 118 mg./L. The average total polysaccharide was moderately elevated, but its ratio to the total protein of 2.15 ± 0.64 is lower than the control value of 2.74 ± 0.89; however the difference is not significant.

Convulsive disorders. There were 18 patients in this category. Ten were classified as having idiopathic or essential epilepsy, and the remaining eight were diagnosed as having symptomatic or acquired epilepsy, based on the criteria of Forster.[12] In the symptomatic group, five of the eight had histories of significant head injury, two had focal seizures, and in the remaining patient the seizures started at the age of 57 years.

Idiopathic epilepsy. This group had the lowest average total polysaccharide content in the spinal fluid, 13.1 ± 3.7 mg./L. The average ratio of 3.09 ± 0.98 does not differ significantly from the control.

Symptomatic epilepsy. While the average total polysaccharide is higher than the control, it still shows very wide deviations. The ratio is significantly increased over the control.

Other miscellaneous neurologic diseases. The spinal fluids from 20 patients

TABLE 2

AVERAGE RATIOS OF TOTAL POLYSACCHARIDE TO TOTAL PROTEIN IN CEREBROSPINAL FLUID

Disease	*No. of Cases*	*Average Ratio Total Polysaccharide Total Protein x100*	*P*
Control	15	2.74 ± 0.89	
Multiple sclerosis	25	3.82 ± 1.74	0.05
Neurosyphilis	24	4.12 ± 1.56	0.001
Brain tumors	16	5.02 ± 2.44	0.001
Cerebral thrombosis	6	4.70 ± 1.15	0.001
Infectious neuritis	5	2.15 ± 0.64	0.20
Idiopathic epilepsy	10	3.09 ± 0.98	0.30
Symptomatic epilepsy	8	4.03 ± 2.28	0.05

with miscellaneous neurologic disorders were studied. This group included such conditions as familial cerebellar degeneration, vitamin B deficiency polyneuritis, Tay Sach's disease, herniated lumbar intervertebral disk, cerebral atrophy with alcoholism, congenital communicating hydrocephalus, idiopathic and postencephalitic parkinsonism, and syringomyelia. In many of these cases the spinal fluids could be considered normal as far as the cell counts, total protein, chloride and glucose contents, the colloidal gold curve, and the serology were concerned. The average total protein was 350 ± 208 mg./L. The total polysaccharide values ranged from 9.0 to 35.0 mg./L. The ratios ranged from 1.74 to 7.45. In nine of the 20 cases the ratios were above the upper limit of the control value, while the total protein values were well within the average control value.

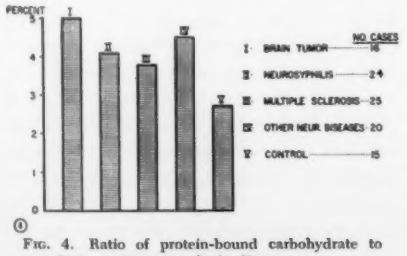

FIG. 4. Ratio of protein-bound carbohydrate to protein in various neurologic diseases.

Infections of the nervous system. A case of torula meningitis and a case of viral encephalitis of undetermined type were studied. In the torula meningitis the spinal fluid had a total polysaccharide content of 93.0 mg./L. and a total protein level of 3,860 mg./L. The ratio was 2.44. In the case of viral encephalitis the total polysaccharide of the spinal fluid was 57.9 mg./L., the total protein was 1.370 mg./L., and the ratio was 4.23. Here it can be seen that, in spite of the higher total protein content of the spinal fluid in torula meningitis, the ratio is lower than that of the viral encephalitis and even falls within the range of the control value.

Pregnancy. In view of the finding of elevated serum protein-bound carbohydrates in this condition,[7] we determined the total polysaccharide content of the spinal fluid in order to determine if it is also increased. Spinal fluids taken during spinal anesthesia from six pregnant women were studied. Five underwent cesarean section during the last month of pregnancy, while the sixth patient underwent a dilatation and curettage for

TABLE 3

GAMMA POLYSACCHARIDE AND GAMMA GLOBULIN IN CEREBROSPINAL FLUID

Disease	*No. of Cases*	*Average Gamma Polysaccharide*	*Average Gamma Globulin mg./L.*	*Average Ratio G. Polysaccharide G. Globulin x100*	*P*
Non-demyelinating conditions	10	1.8 ± 0.8	37.2 ± 15.0	4.84 ± 2.81	
Multiple sclerosis	21	8.9 ± 4.6	129.0 ± 60.3	6.90 ± 3.23	0.05
Neurosyphilis	26	8.0 ± 2.5	151.0 ± 55	6.90 ± 3.23	0.70

abortion during the third month of gestation. The average total polysaccharide was 15.2 ± 6.1 mg./L., the average total protein was 404 ± 59.3 mg./L., with a ratio of 3.76 ± 1.46. This ratio is significantly increased over the control with a "P" value of 0.05.

Gamma Polysaccharide and Gamma Globulin Content of the Spinal Fluid

Since gamma globulin has been found to be consistently elevated in the spinal fluid of patients with multiple sclerosis and neurosyphilis,[9,13] we extended our studies to this protein and its bound carbohydrate. For comparison we used the average values of gamma polysaccharide and gamma globulin and their ratios in the spinal fluids from ten patients with nondemyelinating diseases, as determined previously in this laboratory.[14] The gamma globulin content of these fluids averaged 37.2 ± 15.0 mg./L. and is within normal limits.[9,13]

The spinal fluids from 21 patients with multiple sclerosis were studied. Seventeen were in clinical exacerbation and four were in remission. All had elevated gamma globulin levels with an average of 129 ± 60.3 mg./L.

The spinal fluids from 26 cases of neurosyphilis were studied. The average gamma globulin content was 151 ± 55 mg./L.

The average values for the gamma polysaccharide, gamma globulin, and their ratios are shown in table 3. It can be seen that the gamma polysaccharide and gamma globulin values are markedly increased in multiple sclerosis and in neurosyphilis, as compared with the nondemyelinating diseases. However, the ratio is increased significantly only in multiple sclerosis.

DISCUSSION

The total polysaccharide in the spinal fluid shows the greatest increase in brain tumors, as compared to the control and other neurologic diseases. This is well illustrated in figure 1. In other neurologic conditions, with the exception of idiopathic epilepsy, a moderate elevation of the protein-bound carbohydrates was obtained. On the other hand, the total protein content is highest in infectious polyneuritis, while it is only moderately elevated in the brain tumors. In the other neurologic diseases it does not deviate significantly from the control group. The lowest ratio of total polysaccharide to total protein is found in infectious polyneuritis, which has the highest total protein value. As compared with the control, in some neurologic diseases where the average total protein is lower and the average total polysaccharide is higher, their ratios are significantly increased. The increase of the total polysaccharide in these fluids cannot then be related merely to the increase of the total protein content. We have to assume that there is a selective elevation

in the protein fraction, or fractions, especially rich in bound carbohydrates.

Stary and co-workers[15] determined the glycoproteins in the normal spinal fluid with the orcinol method after precipitation by trichoracetic acid. Since this method did not include the seromucoid fraction of the glycoproteins, their values are lower than those of our control group.

Paper electrophoretic studies on spinal fluid glycoproteins[16,17] have shown that the greatest percentage of the bound carbohydrates are associated with the alpha and beta globulin, to a lesser degree with gamma globulin, and very little with albumin. An increase of these carbohydrate-rich fractions without a corresponding increase of the carbohydrate-poor proteins could very well result in an elevation of the ratio of the bound carbohydrates to the total protein content. This increased ratio could occur even with a normal total protein value.

Paper electrophoretic studies of the spinal fluid proteins in brain tumors by Cumings[18] have shown an increase of the beta globulin. His studies on brain tumor extracts suggested that this fraction originates from the growth itself. In neurosyphilis and multiple sclerosis the increase of gamma globulin in the spinal fluid is well established.[9,13] In multiple sclerosis an increase of the beta globulin has also been reported.[19] The increase of these protein fractions which are high in bound polysaccharides could account for the increase of the total polysaccharide vs. total protein ratios in these three conditions.

In infectious polyneuritis, on the other hand, paper electrophoretic studies on the spinal fluid proteins[20] have shown patterns similar to the normal fluid, with an increase of the albumin in relation to the total proteins. The increase of this fraction which carries a very low carbohydrate content could explain the low ratio in this condition. This is also true for idiopathic epilepsy where the electrophoretic pattern of the spinal fluid proteins is within normal limits.[21] All these are in agreement with our findings.

The origin of the glycoproteins in the spinal fluid is related closely to the origin of the proteins. Evidence has been presented[22] that the spinal fluid proteins are derived from the blood. Other workers[23] have found indications that in pathologic conditions some of these proteins are synthetized within the nervous system. We have determined the total polysaccharide and total protein content in the lumbar and ventricular fluids from a patient with an astrocytoma of the occipital lobe. In the ventricular fluid the total polysaccharide was 13.5 mg./L., the total protein was 430 mg./L., and the ratio was 3.14. In contrast, in the lumbar fluid the total polysaccharide was 120.0 mg./L., the total protein was 1,159 mg./L., and the ratio was 7.55. As can be seen, all the values in the lumbar fluid are greatly increased over those of the ventricular fluid, with the differences far more than those reported.[24] The marked increase of the ratio in the lumbar fluid indicates a selective accumulation of carbohydrate-rich proteins. This would indicate that the tumor contributes in part to the increase of the protein-bound carbohydrates.

Since the total polysaccharide in the serum of brain tumor patients has been reported to be elevated,[5] we studied the relationship between the serum and spinal fluid protein-bound carbohydrates in a patient with an astrocytoma of the temporal lobe. In the spinal fluid the

total polysaccharide was 20.0 mg./L., the total protein was 528 mg./L., and their ratio was 3.79. The total polysaccharide and its ratio to the total protein are increased as compared to the control values. In the blood the total polysaccharide was 163.0 mg. per cent and its ratio to the total protein was 2.90. These values are increased as compared with those of normal blood,[5] where the total polysaccharide averaged 110 ± 15 mg. per cent and its ratio to the total protein was 1.60. These findings suggest that the increase of the total polysaccharide in the spinal fluid could be the result of an overflow from the elevated blood glycoproteins, but does not exclude the possibility that the increase of the protein-bound carbohydrates in both blood and spinal fluid are manifestations of a generalized alteration in the metabolism of these substances in the body.

The increase of serum glycoproteins has also been reported in degenerative vascular disease[25] and in pregnancy.[7] While it is tempting to draw parallel conclusions here as is done above, we do not have similar data in these two conditions. It is interesting to note that increases of the spinal fluid total polysaccharide occur in cerebral thrombosis where there is mainly destruction of tissue and in tumors where tissue proliferation is predominant.

The persistent elevation of the total polysaccharide/total protein ratios in the spinal fluids of the groups of multiple sclerosis patients in exacerbation and remission suggests that the disease process is continuously active during these two phases. However, these determinations were carried out in groups of patients during these two phases of the disease. Since it has been found that the gamma globulin content of the spinal fluid has risen during exacerbation and fallen during remission,[26] ideally the total polysaccharide content of the spinal fluid in the same patient during these stages of the disease should be investigated in order to clarify the changes that occur.

It has been shown by these studies that in various neurologic diseases where the spinal fluid has been considered normal, the total polysaccharide and its relationship to the total protein is often significantly increased. This determination could then be considered as a more sensitive index for organic changes than the usual tests of cell count, total protein, chloride and glucose contents, and the colloidal gold curve.

A significant increase of the ratio between the gamma polysaccharide and the gamma globulin has been found in experimental infection and immunization.[27] Obviously here the increased ratio is a manifestation of antibody formation. While the rise of the gamma globulin and its bound carbohydrate in neurosyphilis is due to antibody formation against the causative organism, this relationship does not hold for multiple sclerosis where an infectious etiology is very unlikely.[28] The significance of the increased ratio in multiple sclerosis awaits further study.

The determination of the polysaccharide and its ratio to the protein in the spinal fluid can be of definite diagnostic aid in neurologic diseases, especially brain tumors. It would also be useful in assaying the organicity of seemingly functional complaints. Further study on the fractionation of the spinal fluid glycoproteins and examination of their carbohydrate contents is needed to establish whether they increase in different

patterns which might be characteristic of certain neurologic diseases.

SUMMARY

1. Total polysaccharide and total protein and their ratios were determined in the spinal fluids from 129 patients with various neurologic disorders. The spinal fluids from 15 patients with non-neurologic diseases were used as controls.

2. The greatest increase of the total polysaccharide is found in brain tumors. The total polysaccharide content is moderately increased in the spinal fluid of patients with multiple sclerosis, neurosyphilis, cerebral thrombosis, symptomatic epilepsy, infectious polyneuritis, and other neurologic diseases. It is not increased in idiopathic epilepsy.

3. The ratio of the total polysaccharide to the total protein is increased significantly but in varying degrees in brain tumors, multiple sclerosis, neurosyphilis, and cerebral thrombosis, while it is not increased in idiopathic epilepsy and infectious polyneuritis.

4. The gamma polysaccharide and gamma globulin content of the spinal fluid and their relationships were determined in multiple sclerosis and neurosyphilis. The gamma globulin and gamma polysaccharides are markedly increased in these two diseases as compared to non-demyelinating conditions. The ratio of the gamma polysaccharide to the gamma globulin in multiple sclerosis is significantly increased.

5. The significance and probable mechanisms of these changes are discussed.

6. The clinical application of these procedures is evaluated.

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■ The small number of fibres in the anterior pyramids, on the one hand, has appeared to be insufficient for the conveyance of the orders of the will to all the muscles of the trunk and limbs; and the existence of paralysis on the side injured in the encephalon, on the other hand, has contributed to lead to the actually admitted opinion that the voluntary motor fibres make a part of their decussation in the medulla oblongata, and the other part in the pons Varolii, and also higher up between the two sets of tubercula quadrigemina and the two cerebral peduncles. Long ago Cruveilhier had said that "the small fascicles, called anterior pyramids, cannot be sufficient for the extensive phenomena indicating a crossing of action in the brain." A man of great authority in physiology as well as in pathology, Dr. R. B. Todd, says that "anatomy suggests that a lesion limited to either anterior pyramid would affect the opposite side of the trunk, for it is known that such an effect follows disease of the continuation of it in the meso-cephale or crus cerebri; and that lesions limited to the potserior half of the medulla oblongata, on either side, would affect the same side of the body, no decussation existing between the fibres of opposite restiform or posterior pyramidal bodies."

C. E. Brown-Séquard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

Hearing and Speech in Infantile Hemiplegia Before and After Left Hemispherectomy

*Robert Goldstein, Ph.D., Allan C. Goodman, Ph.D. and Robert B. King, M.D.**

ALTHOUGH about 50 cases have been described in which hemispherectomy has been performed on patients with infantile hemiplegia, there has been little discussion of quantitative measures of auditory function in these patients. The qualitative descriptions indicate, however, that auditory thresholds and understanding of speech were normal prior to and following surgery.

While the cerebral abnormality which led to infantile hemiplegia did not disturb the speech and language of most of the patients, it prevented a few of them from developing useful speech.[1-3] Removal of the abnormal cerebral hemisphere did not further impair the speech of the patients. Occasionally there was improvement in the ability to speak.[1,2]

We shall present quantitative findings on the hearing of four patients and a discussion of the speech of these patients.

CLINICAL DESCRIPTION

All four patients had right hemiplegia from infancy or early childhood. Their ages at time of the hemispherectomy were 12½, 30, 35, and 37. All four had had generalized seizures; two of them also had focal seizures. One patient had frequent seizures at the time of hospitalization.

The intelligence quotients of the patients on the full-scale Wechsler-Bellevue test were 43, 58, 61, and 97 preoperatively, and 54, 67, and 65 postoperatively. The fourth patient was not tested postoperatively. The general behavior of all four patients, however, was indicative of considerably greater intellectual capacity than is implied by each of their scores. The most intelligent of the group completed two years of college. Her education was interrupted because of uncontrolled seizures. The others had only two to four years of primary schooling.

All four patients had severe and paroxysmal behavioral disorders. They were forgetful, belligerent, assaultive, and destructive, and were susceptible to apparently unprovoked outbursts of violent rage. Two of the patients had been hos-

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*Markle Scholar in Medical Science.

TABLE 1.
DETAILED RESULTS OF HEARING TESTS BEFORE AND AFTER LEFT HEMISPHERECTOMY

CASE		THRESHOLD LOSS									DISCRIMINATION LOSS	
		Pure Tones								*Speech*		
		250	500	1000	2000	3000	4000	6000	8000	W-2†	RH*	W-22**
1	R– Pre	0	–5	0	–5	0	10	15	15	1	36% 52%	
	Post	10	5	5	0	–10	10	25	10	0	42% 54%	16%
	L– Pre	–10	–5	0	–10	5	10	0	10	3	24% 30%	
	Post	–5	–10	–5	–5	5	10	10	20	6	16% 46%	8%
2	R– Pre	–5	0	0	0	5	5	0	0	–2	38% 30%	
	Post	–10	–10	–10	–5	–5	–5	–5	–10	2	28% 36%	4%
	L– Pre	5	5	–5	–5	0	0	0	–5	3	16%	
	Post	–10	–10	–10	–10	–10	–5	20	–5	–2	18% 20%	4%
3	R– Pre	10	10	5	5	10	10	0	10			
	Post	–10	–10	–10	0	10	15	0	10	8	50% 42%	18%
	L– Pre	15	15	10	5	10	60	25	10			
	Post	5	5	–5	–5	0	45	40	20	5	18%	0%
4	R– Pre	–5	–5	–5	5	10	5	5	5	2	44% 44%	
	Post	–5	0	0	0	15	10	20	25	3	46% 60%	
	L– Pre	0	–10	–5	–10	–10	–10	–5	0	–4	18%	
	Post	5	0	0	0	10	10	15	20	–1	18%	

†Spondiac words. Recorded version: *CID Auditory Test W-2.*
*Monosyllabic words. Recorded version: Rush Hughes recording of the Psycho-Acoustic Laboratory's phonetically balanced lists of 50 words.
**Monosyllabic words. Recorded version: *CID Auditory Test W-22.* Ira J. Hirsch recording of modified form of the Psycho-Acoustic Laboratory's phonetically balanced lists.

pitalized for a number of years; the other two were seen in consultation as a final step prior to their being institutionalized for behavioral disorders. Hemispherectomy was recommended primarily in an effort to bring about improvement in behavior, and also in one case to control frequent, severe seizures.

The entire cortex of the abnormal hemisphere was removed, and in two cases the head of the caudate nucleus was removed. The thalamus and lentiform nuclei were carefully excluded from the resected tissue.

A more detailed description of the neurologic findings and behavior in these four patients before and after hemispherectomy will be described in a later report.

HEARING AND SPEECH

Tests of hearing were performed pre- and postoperatively. The speech of one patient was recorded prior to surgery; the speech of all four patients was recorded postoperatively. These studies were made in the intervals between violent outbursts by the patients. The patients were cooperative and the results of the tests are reliable.

HEARING

In assessing the hearing of these patients, we were concerned primarily with measurements of threshold and of discrimination.

We determined the threshold for pure tones ranging in frequency from 250 to 8,000 cycles per second. We lowered and raised the intensity of each tone until we found the intensity of the sound which could just be heard and recorded this level as the threshold.

For measuring the threshold of intelligibility for speech, we used bisyllabic words with equal stress on each syllable (spondees). We used a recorded version of the test known as CID Auditory Test W-2.[4] The words were presented to one ear at a time through earphones. The intensity of the recorded speech was gradually reduced until a level was found below which the patients could not repeat half of the words correctly. This level was recorded as the threshold.

In clinical audiometry, any threshold ten decibels below (−10) or ten decibels above (10) normal threshold (0) is considered to be within the normal range. Thus, according to the data in table 1, none of our patients suffered a significant loss of sensitivity either for pure tones or for speech. We do not attribute any significance, as far as the cerebral damage or hemispherectomy is concerned, to the relatively small hearing losses for the high frequencies.

In the test of the discrimination for speech, monosyllabic words are presented to the listener at an intensity sufficiently above his threshold so that all the words are loud enough to be heard comfortably. The words are again presented to one ear at a time through earphones. Results of the test can be expressed in terms of "discrimination loss," that is, in percentage of words incorrectly identified or missed entirely.

Each list of 50 words used for this purpose is phonetically balanced with regard to the frequency of occurrence of the various phonetic elements of the English language.[5] In general, it is more difficult to identify the monosyllabic words correctly than it is to identify the bisyllabic words used in measuring the threshold of intelligibility for speech.

We used two recorded versions of the phonetically balanced lists of words. One will be designated RH and the

other W-22[4] (see table 1). Almost invariably, more words are incorrectly identified with the RH version than with the W-22 version.[6] The lists of words used in both sets of recordings are similar. The important difference between the two versions, which probably accounts for the difference in difficulty, is that the speaker in the RH version enunciates his words much less distinctly than the speaker in the W-22 version. Although in general these monosyllabic words are more difficult to identify than are the bisyllabic words used in testing the threshold of intelligibility for speech, a person with normal hearing will not miss more than 20 per cent of words in the RH version and usually not more than 5 or 10 per cent. Persons with normal hearing seldom miss more than 5 per cent in the W-22 version.

In all instances the level of speech delivered to the ear of the listener was approximately 70 decibels above his threshold of intelligibility for speech, as determined by the W-2 (spondee) test. Although it is usually recommended that the words be presented only 30 to 40 decibels above this threshold, we find that patients prefer a louder voice for comfortable listening.

In spite of the normal thresholds, there seemed to be a significant impairment in discrimination for the words in the RH test. On the average 45 per cent of the words were either incorrectly identified or missed in the right ear, the ear contralateral to the pathologic hemisphere, compared to an error of 20 per cent in the left ear, the ear contralateral to the intact hemisphere. The discrimination loss of 20 per cent in the left ear may or may not be within the normal range. Although the scores on the W-22 test were within the normal range, they also indicated poorer discrimination in the right ear than in the left in two of three patients.

The measured impairment in the discrimination of speech has a parallel in the report of three of the patients on the distinctness of the speech presented to each ear. Two of the patients volunteered after the tests of discrimination that the words sounded "clearer" in the left ear than they did in the right. A third patient made the same comment when asked about the clarity of the speech. A fourth patient (No. 1) did not note any difference in clarity. The patients commented, when questioned, that even the pure tones did not sound as clear in the right ear.

Because of the uniformity of the findings, the results from all of these hearing tests have been summarized in table 2.

TABLE 2.
SUMMARY OF HEARING TESTS BEFORE AND AFTER LEFT HEMISPHERECTOMY

	THRESHOLDS		DISCRIMINATION	
	Pure Tones	*Speech (W-2)*	*RH*	*W-22*
Left Ear	Normal	Normal	20% Error (normal?)	4% Error (Normal)
Right Ear	Normal	Normal	45% Error (abnormal)	13% Error (Normal?)

SPEECH

The speech of the patients, while somewhat lacking in proper control of loudness or tempo, gave no evidence of aphasia. However, we did not administer any formal tests which might have revealed disturbances of language that were not apparent in ordinary conversation. Vocabulary and language seemed commensurate with apparent intellectual ability and level of education.

Although we recorded the speech of only one patient (No. 4) before hemispherectomy to compare with records made postoperatively, it was apparent that speech was not adversely affected by the surgery. We observed uniform improvement in the modulation of speech in three patients.

One of the patients (No. 1) gave bizarre responses during the hearing tests in the postoperative session. During the test of the threshold of intelligibility for speech, he replied not simply with the word presented to him but would use that word in a phrase or sentence. For instance, in response to the word "airplane," he said "airplane takes off from the ground." During the test of the discrimination for speech, the patient would often reply with a word associated with the word presented. For example, for "have" he said "given," for "arm" he said "hand," and for "wave" he said "water." We had to repeat the instructions for replying before he began repeating the exact word that was said to him. During another part of the test he added the sound "ee" to each of the words: he said "huggy" for "hug," "chappy" for "chap," "tiley" for "tile," and so on.

DISCUSSION

The results of the auditory tests on these four patients with right infantile hemiplegia before and after left hemispherectomy confirm quantitatively the qualitative observations made previously in other similar cases. We have added the observation of impaired ability to understand somewhat distorted speech in spite of normal thresholds for pure tones and speech. This impairment is marked in the ear contralateral to the pathologic hemisphere and did not change after hemispherectomy.

Bocca and others[7] in Italy reported similar findings in cases of unilateral temporal lobe tumor. For their test of discrimination for speech, they distorted speech by filtering out most of the high-frequency components. Sixty to 80 per cent of this distorted speech was understood correctly by "normal subjects." The patients with tumors of the temporal lobe, however, missed a larger percentage of the words even though they, too, had normal thresholds. In 13 of 14 cases, more words were missed when presented to the ear contralateral to the pathologic temporal lobe than when delivered to the ear contralateral to the intact temporal lobe. The impairment in discrimination in both ears diminished or disappeared, however, in 20 to 30 days following excision of the affected temporal lobe.

It is impossible to determine from existing studies whether specific lesions in the temporal lobe are responsible for the impairment in discrimination, or whether damage to cerebral tissue in general is responsible. Bocca and others[7] did, however, point out that, when preoperative tests failed to show an impairment of discrimination for distorted speech, the tumor did not involve the "auditory area" of the temporal lobe. When the "auditory area" was removed with other affected portions of the cortex, in these

cases discrimination was affected. It will be necessary to test auditory function in many patients with localized cerebral lesions other than in the temporal lobe to resolve this question.

Bilateral representation of auditory stimuli in the cerebral cortex has been described,[8] and our studies of thresholds for pure tones and speech tend to support this concept. The results of our tests of the discrimination for speech with the RH test suggest that cerebral mechanisms for this degree of discrimination may have a major representation in the hemisphere contralateral to the ear tested. Because discrimination did not improve in either ear following left hemispherectomy, it would appear that the preoperative impairment did not result from a nociferous influence of remote abnormal cortex on supposedly normal cortex. These observations may reflect primarily a discriminatory deficit which may be common to other sensory modalities and do not represent simply an auditory abnormality.

Our observations on the speech of patients with right infantile hemiplegia before and after hemispherectomy confirm the majority of observations previously reported. The improvement we noted in the speech of these patients accompanied a much more striking improvement in their general behavior. The improvements following surgery suggest that abnormal activity in the pathologic hemisphere may disrupt the functioning of the intact hemisphere.[1,9] Removal of the left hemisphere may have removed the disrupting influences on the right hemisphere so that perhaps speech, as a reflection of the improved behavior, was more nearly normal. For this reason we do not suggest that the hemispherectomy had a primary influence on speech as such in these patients.

We cannot contribute to the understanding of the problem of handedness and cerebral dominance, because all four of the patients were compelled by their hemiplegia to be left-handed from early childhood. If we accept the conclusion[10,11] that "left-brainedness" occurs in the large majority of the population, then our findings can serve as a partial confirmation of the ditcum[12] that, if there is damage to the dominant cerebral hemisphere at a very early age, the other hemisphere will assume control of the functions of speech and language.

SUMMARY

Auditory tests were performed on four patients with right infantile hemiplegia before and after removal of the abnormal left cerebral hemisphere. Recording of the speech of one patient was made preoperatively and of all four patients postoperatively.

Preoperative testing showed normal thresholds in both ears for pure tones and for speech. By contrast, the ability to identify relatively difficult words presented at intensities above threshold was not normal. About 45 per cent of the words presented to the ear contralateral to the pathologic hemisphere were identified incorrectly, as compared to an incorrect identification of only about 20 per cent of the words presented to the left ear. The audiometric records following hemispherectomy did not differ significantly from the preoperative records.

The patients' speech, while somewhat lacking in proper control of loudness or tempo, gave no evidence of aphasia. Vocabulary and language were commensurate with intellectual capacity and level of education. Speech was not affected adversely by the surgery.

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■ Epilepsy seems to consist essentially in an increased reflex excitability of certain parts of the cerebrospinal axis, and in a loss of the control that, in normal conditions, the will possesses over the reflex faculty. The base of the encephalon, and especially the medulla oblongata, is the most frequent seat of the increase in the reflex excitability, so that this part of the nervous centre is the ordinary seat of epilepsy. The disturbance in the functions of the cerebral lobes, during and immediately after a fit, and in the interparoxysmal periods, is chiefly due to the alterations taking place in the brain during the fits. This hitherto mysterious coincidence of loss of consciousness, or, in other words, loss of function of the cerebral lobes, with an increased action of the base of the encephalon, in a complete epileptic seizure, may now be easily explained. I have tried to show that the same cause that produces the first convulsions in some muscles of the neck, the eye, the larynx, and the face, produces also a contraction of the blood vessels of the brain proper, which contraction is necessarily followed by the loss of consciousness. I am happy to state that two very able German experimenters – Messrs. Kussmaul and Tenner – led by researches in several respects different from mine, have arrived at the same explanation.

C. E. Brown-Séquard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

Familial Cerebello-Olivary Degeneration with Late Development of Rigidity and Dementia

*Harold R. Carter, M.D. and Chantana Sukavajana, M.D.**

THE GROUP of cerebellar degenerations present an intriguing neurologic problem which is still in need of further clarification, despite the masterly descriptions of the older workers and the present revival of interest in the subject.

In his recent monograph, Greenfield[1] has pointed out how unsatisfactory is the term, Marie's ataxia, and he has emphasized the absence of any pathologic basis which might distinguish this condition. More outspoken was Holmes[2] stating, "Under the term hereditary cerebellar ataxia many cases have been described without any regard to the exact nature and localization of the pathologic lesions." Relevant also is his observation that "Marie attempted to define a new clinical type by collating the cases which had been published by Fraser,[3] Brown,[4] Nonne,[5] and Klippel and Durante,[6] and that when his paper was originally published, he himself had not observed any case which he could include in it. At that time the nature of the disease had been determined by postmortem examination in two only of these cases." Nevertheless, the term is still employed.[7]

From his studies, Greenfield concluded that there are two main types of hereditary cerebellar ataxia, both presenting in a rather uniform manner with the onset of progressive disequilibration in middle age. The cortical cerebellar atrophies are characterized pathologically by marked loss of Purkinje cells, especially in the superior vermis. The prototype of this group is the familial form described by Holmes[8] and is clearly cerebellofugal. The other type, described by Menzel[9] in familial form and later in sporadic form by Déjerine and Thomas[10] as olivopontocerebellar degeneration, shows loss of Purkinje cells, more marked in the hemispheres than the vermis, and degeneration of pontine nuclei and middle cerebellar peduncles. Here the distribution of the lesions is cerebellopetal.

Hereditary cerebellar disease of either variety may be accompanied by involvement of basal nuclei, and this is illustrated by the present paper which is concerned with a Spanish-American family of 19 children, several of whom developed disturbance of gait, ataxia, trem-

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Dr. Carter died unexpectedly during the preparation of this paper, which was completed by Drs. G. Milton Shy and James W. Stephens.

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ors, and speech difficulty in late childhood. The father appeared to have transmitted this tendency, since he developed a similar condition at 44 years of age. This report describes the clinical findings in the father and six afflicted children, three of whom died of the disease. The results of two postmortem examinations are presented.

REPORT OF CASES

Case 1. P.O.R. (Father). This patient was first seen in 1946 at the age of 47. At this time he complained of difficulty in walking for four years and described his gait, particularly when fatigued, as that of a drunken man.

Examination revealed a combination of disequilibration and ataxia. He walked on a wide base, falling indiscriminately to right or left; in addition, there was demonstrable ataxia in the left arm and leg as shown by slowness and irregularity of rapidly alternating and repeated tapping movements. The finger-nose and heel-knee-shin tests confirmed errors in rate, range, direction, and force. Nystagmus was not present. There was no evidence of spasticity, but the left knee jerk was somewhat increased and the plantar response extensor in type. General examination revealed nothing of significance. The cerebrospinal fluid was normal.

During the next four years the patient's condition deteriorated steadily, and by 1951 a moderate degree of organic dementia was present which necessitated commitment to a mental hospital. He was alternately apathetic and irascible without cause, with gross impairment of recent memory, judgment, and criticism. He sat in a fixed posture reminiscent of a parkinsonian immobility, unblinking, and with few spontaneous movements of the eyes. Saliva drooled from the mouth, and his speech was slurred and syllabic in quality. The head showed a rhythmic to-and-fro titubation at three to five cycles per second. The rest of the cranial nerves showed no abnormality, except for a rapid palatal nystagmus. The previously noted ataxia and disequilibration were now almost totally disabling, and there was marked tremor in both upper limbs on attempting volitional movement. The limbs showed a considerable degree of plastic rigidity. The reflexes were very difficult to obtain, but no asymmetry was noted and the plantar responses were flexor. No definite alteration in any sensory modality was observed.

When last seen in 1954, there had been further deterioration. The patient was grossly demented, bedridden, and unable to feed himself due to severe ataxia of the upper limbs. Death occurred that year.

Case 2. J.U.L. This case, the eldest child of case 1, commenced his illness in 1936 at the age of 15. The initial complaint was of progressive awkwardness at first in the legs and later in the arms. When first seen at the age of 20, there was marked generalized ataxia on volitional movement, with an irregular, jerky staccato speech. The cranial nerves, motor, and sensory systems were otherwise intact. Steady deterioration took place in the next four years, with the development of a generalized plastic rigidity and the presence of increased though symmetric deep reflexes and bilateral extensor plantar responses. The face was expressionless, with open, drooling mouth, and the speech was now slow and slurred but still with an explosive quality to it.

By 1948, age 27, a mild organic dementia was present, and he was admitted to a mental hospital; he died there at the age of 30. During the terminal phase of his illness he was bedridden and immobile, with gross generalized rigidity and violent ataxia on attempted movement. His occasional utterances were quite unintelligible, and there was considerable mental deterioration. Nystagmus was not noted at any time.

Case 3. C.H.R. This patient, the eldest daughter, was seen in 1946 with a history of gradual onset of unsteadiness in walking since the age of 14. Examination showed a generalized rigidity of moderate degree. Her gait was bizarre, combining propulsive features with ataxia. She walked rapidly in an attitude of general flexion, with her arms spread out sideways and swinging wildly as if in an attempt to balance herself. Irregular, coarse action tremors were present in all limbs. The expression was one of fixed fatuity, with considerable drooling of saliva, and a slurred dysarthria was noted. No nystagmus was seen.

By 1950 the patient was demented, bedridden, and attempts at speech were completely unintelligible. There was marked generalized rigidity with extensor plantar responses. Death occurred in this year from bronchopneumonia.

Case 4. P.E.R. This patient was seen in 1951 at 21 years of age. He was serving in the United States Marine Corps as an instructor in swimming. He complained that from time to time his hands were shaky and clumsy on movement and that occasionally he staggered and his whole body felt unsteady.

Examination showed only some awkwardness and unsteadiness of the right leg, with no other signs in the nervous system.

Case 5. F.R.E. This case was the second eldest son and the first in the family to develop the disease. At the age of seven in 1929 he developed difficulty in walking which progressed so that by the age of nine, he exhibited a wide-based steppage gait with some ataxia on formal testing but no other definite signs in the nervous system. Tremor of the hands, progressive rigidity, and dementia ensued, leading to death at the age of 11. Unfortunately no autopsy was obtained.

Case 6. S.I.L. At the age of 11 in 1946 this boy complained of dizziness and difficulty in walking and showed a mild unsteadiness of gait. There was no intellectual deterioration.

During the next three years there was progression of his symptoms so that by 1949, in addition to generalized ataxia, there was mental dulling and the appearance of a plastic rigidity, particularly in the left arm. The face became expressionless and a static tremor of the right arm and leg developed. At this time impairment of the extraocular movements occurred, which progressed in the next two years to complete external ophthalmoplegia.

In 1952 dysarthria and drooling of saliva were severe, wild ataxia was present on attempted movement of any extremity, and at rest there were coarse static tremors of all limbs. When last seen in 1955, there had been further slow deterioration.

Case 7. L.A.W. This patient was seen at the age of 12 in 1951, when he presented with mild, generalized, symmetric ataxia. No alteration of reflexes was observed, and there was no nystagmus at this time. When last seen in 1955, there had been no progression of his symptoms.

In general, therefore, the symptomatology of the disease unfolded in a stereotyped pattern, the initial symptom in all cases being disequilibration with awkwardness and unsteadiness on walking. This was followed sooner or later, and in the children this occurred earlier than in the father, by the appearance of rigidity and dementia, usually the rigidity preceding the dementia by a short period. At this time the cerebellar signs were much more marked and were accompanied by speech disturbances. It was noted that nystagmus did not appear, but in one case there was limitation of external ocular movements leading to complete external ophthalmoplegia.

PATHOLOGIC DESCRIPTION OF CASES

Case 3. The central nervous system showed the following gross findings: The weight of the brain was 780 grams; that of the cerebellum was 60 grams. The cerebrum showed marked diffuse atrophy. The external configuration was normal. The deep white matter along the corpus callosum was increased in consistency. There were no gross lesions in the basal ganglia. The cerebellum was greatly atrophic and the folia were shrunken. The pons and medulla were somewhat reduced in size. The spinal cord appeared grossly normal.

Microscopically the cerebral cortex exhibited diffuse atrophy on examination with Nissl stain. The stratification was indistinct. The nerve cells were packed closely together due to decreased intercellular substance. In some fields the third and fifth layers were poor in cells. The thickness of the cortex showed reduction to one-third of normal in some areas. The nerve cells in general were in good condition, aside from mild degenerative changes. Blanching of neurons and ghost cells was seen in several instances. On the whole, there was very little glial activity. The protoplasmic astrocytes were somewhat increased in number and occasional nuclei were enlarged. The picture in all cortical areas examined was essentially the same. The white matter showed a mild degree of demyelination. The number of large nerve cells in the corpus striatum was slightly reduced.

The cellular pattern in the nucleus ventralis lateralis of the thalamus was somewhat irregular, and there were small patches with outfall of nerve cells and a few ghost cells. This was accompanied by mild proferation of astrocytes

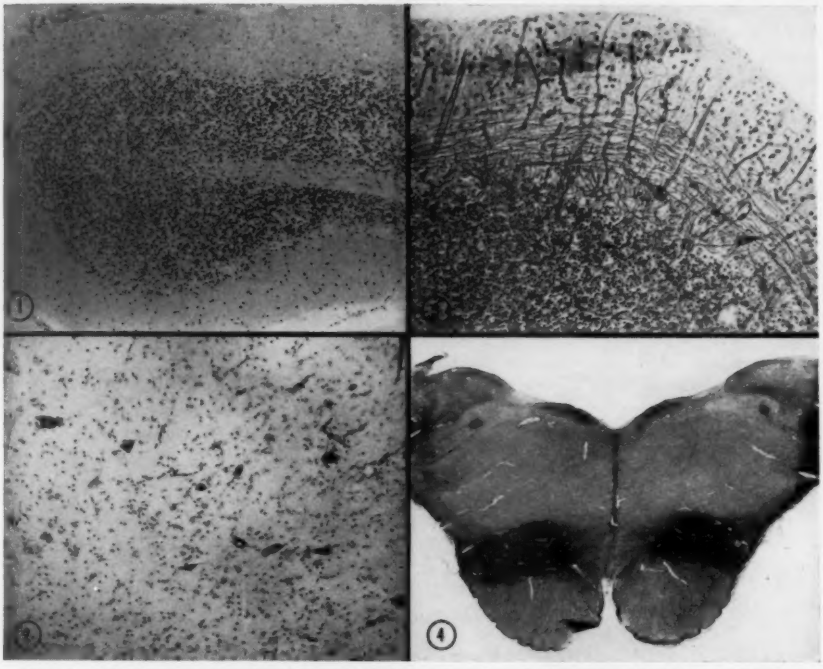

FIG. 1. Cerebellar cortex showing absence of Purkinje cells and rarefaction of granular layer. Nissl stain.
FIG. 2. Substantia nigra showing outfall of pigmented nerve cells. Nissl stain.
FIG. 3. Cerebellar cortex showing empty baskets. Von Braunmuehl silver stain.
FIG. 4. Gliosis of inferior olivary nuclei. Phosphotungstic acid hematoxylin stain.

and oligodendroglia cells. There were, however, numerous well preserved cells.

The most conspicuous lesions were found in the cerebellum. The molecular layer was thin but free of abnormal glial reactions. The majority of Purkinje cells had disappeared (figure 1). Some of the remaining ones were in good condition; others were very small and had light, indistinct cytoplasm and dark nuclei. Silver stain failed to reveal the baskets of the missing Purkinje cells, and nerve fibers were poorly represented throughout the cerebellum. Only the transverse fibers connecting the basket cells were better preserved. The thickness of the granular layer was reduced to one-third or one-fourth of normal. The individual granule cells appeared normal but widely separated from each other. The subcortical white matter exhibited degeneration with a moderate degree of protoplasmic and fibrillary gliosis. The dentate nuclei were well preserved; the astrocytes were more numerous and somewhat larger than normal. The olivary nuclei exhibited nearly complete loss of ganglion cells; only one or two were preserved in a low-power field; there was a moderate proliferation of protoplasmic glia. The intra- and periolivary myelinated fibers were degenerated. The pyramidal tracts and external arcuate fibers were not involved. The pons was smaller than normal, in keeping with the general brain atrophy. The pontine nuclei and fiber masses, however, showed little, if any, evidence of degeneration. Sections of the spinal cord were not satisfactory due to the presence of artifacts; however, serious lesions did not appear to be present.

Case 2. Gross appearance of the brain: The meninges and blood vessels were normal. The

weight of the whole brain was 755 grams, that of the cerebellum 55 grams. The frontal lobes showed a moderate degree of shrinkage of gyri and wide sulci, in contrast to the other lobes. The cerebellum was smaller than normal and showed atrophy of the folia. The pons and medulla oblongata likewise were smaller than normal. The ventricular system and basal ganglia were not remarkable.

Microscopic examination: The cerebral cortex showed diffuse atrophy, especially in the frontal lobes. The stratification was indistinct in some convolutions. Elsewhere, band-shaped outfall was seen in the third and fifth layers. Most of the ganglion cells showed nonspecific degenerative changes. The white matter showed a mild degree of demyelination throughout, mainly in the frontal lobes. There was slight overgrowth of large protoplasmic astrocytes without gliosis. The globus pallidus showed loss of nerve cells and mild gliosis in some areas. There was a marked loss of pigmented cells in the substantia nigra on both sides with macro- and microglial overgrowth and with extraneuronal scattering of melanin granules (figure 2).

The cerebellar lesions greatly resembled those of the first case, with the following differences: There were practically no well preserved Purkinje cells; the baskets were visible in silver stain (figure 3); the granular layer was somewhat less damaged; and the nerve cells of the dentate nucleus contained some fatty pigment. In the inferior olivary nuclei only a few ganglion cells were left, and there was extensive fibrillary gliosis (figure 4). The intra- and periolivary myelinated fibers were sparse and degenerated. In the pons the number and size of ganglion cells were decreased, and there was protoplasmic and fibrillary gliosis, especially on the right. The pontocerebellar fibers were degenerated and scanty, without glial replacement. The pyramids were normal.

Summary of Pathologic Findings. The outstanding feature of these two cases was the almost complete absence of the Purkinje cells, with preservation of basket fibers. The granular layer was less affected. The neocerebellum and paleocerebellum were equally degenerated. Marked atrophy of the inferior olivary nuclei was present. The cerebral cortex was atrophic. There was loss of pigmented cells in the substantia nigra. Associated with cerebral and cerebellar changes, mainly in the second case, were degenerative changes in cerebellopontine fibers, pontine, and dentate nuclei.

HEREDITARY FACTORS

All of the living children of the "Q" family have been contacted. To date (1955), A.B.R.—age 27, B.E.N.—age 23, M.A.R.—age 21, J.N.O.—age 15, and R.I.C.—age 10, have no complaints and show no signs on physical examination. The mother of this large family is normal in all respects, as are her two brothers and the grandfather, now age 90.

The father's two brothers died in infancy, and the paternal grandfather died at the age of 30 from an accident. As far as is known neither his brother nor his sister showed stigmata of the disease. The paternal grandmother came from a family of eight, none of whom exhibited neurologic disturbances.

A survey of the pedigree chart (figure 5) suggests that the defective genes in this pathologic condition of the nervous system are sex-linked recessive ones which afflicted the father's side. His own father might have been missed because of his premature death. As in so many of the familial ataxias, anticipation was evident so that several children were seen with the disease before the father became afflicted.

DISCUSSION

The syndrome of progressive cerebellar ataxia, familial or sporadic, has been amply documented in the literature. Although Holmes described the familial form of cerebello-olivary degeneration in 1907, there were extant earlier reports of the sporadic variety. Murri[11] described

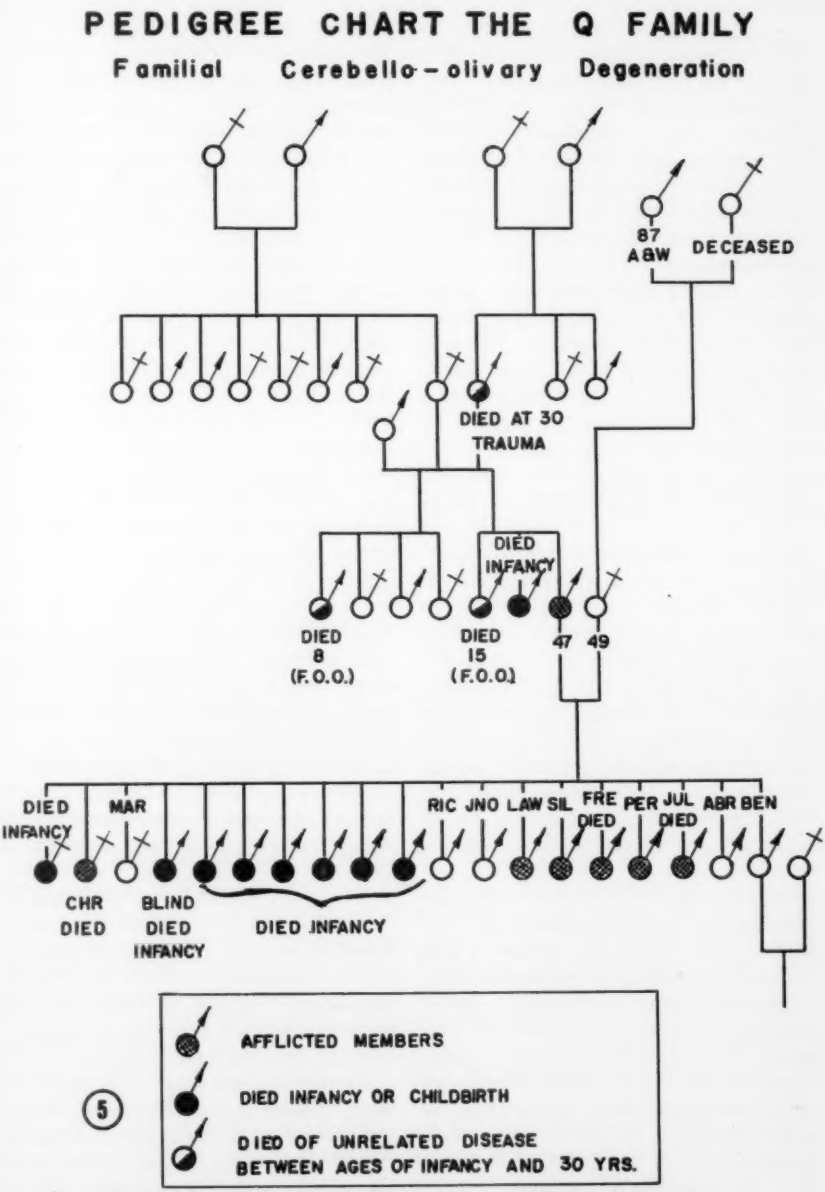

FIG. 5. Pedigree chart of the Q family with familial cerebello-olivary degeneration.

a woman with a cerebellar syndrome which developed during a chronic enteritis and pathologically showed a marked diminution in the number of Purkinje cells, the granular and molecular zones being normal. In 1906 Marie showed a similar case, the pathologic lesions being described by Rossi[12] in 1907. Clinically the course was characterized by disturbances of equilibration with relative integrity of the upper limbs. A special anatomic localization was noted for the first time with the involvement of the anterior and posterior quadrangular lobes, the flocculus, culmen, and declive.

In 1922 there appeared the paper of Marie, Foix, and Alajouanine[13] summarizing the clinical picture with Gallic simplicity: "It is a syndrome of cerebellar deficit, bilateral and symmetrical, of late onset and progressive march characterized principally by a profound disorder of equilibration, in stance, and, above all, in gait. The disorders of coordination are most marked in the legs, the arms may almost escape. Nystagmus appears late, if at all, and the rest of the nervous system is intact." They noted a characteristic distribution of Purkinje cell atrophy. "The lesions diminished from the superior face towards the inferior face, from the midline and the vermis towards the lateral poles, and from the anterior border towards the posterior border of the organ." Curiously, they did not refer to Holmes' paper with similar findings in the familial form.

Sporadic reports continued to appear and various etiologic agents were proposed: Chronic alcoholism,[14–16] virus disease,[17] infection and malnutrition,[18] anoxia,[19] and heatstroke.[20] A more rapidly progressive form has been described in association with carcinoma of the ovary,[21] pancreas,[22] or bronchus.[23]

Clinically this group of cases is neither easily nor constantly distinguished from olivopontocerebellar atrophy. Déjerine and Thomas[10] in their classic description of the latter noted the onset in late middle life of a progressive cerebellar dysfunction affecting the legs predominantly. Histologically there was atrophy of the cerebellar cortex, the hemispheres being more affected than the vermis, associated with atrophy of the pontine nuclei and middle cerebellar peduncles. Intermediate between the cerebello-olivary and the olivopontocerebellar forms were those described by Schroeder and Kirschbaum.[24] In their two cases, in addition to the cortical cerebellar atrophy, there was degeneration of the inferior olives and nucleus dentatus, but sparing of the middle peduncles and nuclei pontis.

Associated degeneration of pyramidal tracts, posterior columns, and spinocerebellar tracts has been observed,[25] and involvement of the basal ganglia while commoner in the olivopontocerebellar variety has been reported in the familial cerebello-olivary degenerations.[26–29]

From this survey there emerges the picture of a group of cerebellar degenerations, familial or sporadic, predominantly affecting cerebellar afferent or efferent systems, with or without associated involvement of the basal ganglia. A strong familial trait is more frequently found in cerebello-olivary degeneration, whereas association with striatal disease and late development of rigidity and other parkinsonian features are more common in the olivopontocerebellar form.

The family described above illustrates many of these points. There was no special incidence of Purkinje cell loss relative to the vermis or the hemispheres, the middle cerebellar peduncles did not

show any abnormality, and the severity of the changes was far more marked in the cerebellum than in the nuclei pontis. On these grounds, it was felt that the picture was more consistent with a cerebellofugal type of atrophy, the decision being made on the distribution of the lesions, although Lichtenstein[30] states that it is only by studying the age and duration of the degenerative process that one may decide where the lesion begins.

The association of either form of cerebellar degeneration with progressive dementia is not unusual. Akelaitis[31] reported two members of a family with parenchymatous atrophy of the cerebellar cortex associated with mental deterioration. Histologically a definite decrease of ganglion cells in the third and fifth layers of the cortex was observed in the frontal and parietal regions, in addition to the Purkinje cell loss in the superior vermis, lingula, lobulus centralis, culmen, and declive. In 1941 Guillain, Bertrand, and Godet-Guillain[32] studied a case of progressive ataxia starting at 17 years of age which during the next 23 years developed speech difficulty, nystagmus, and mental deterioration. In addition to the usual cerebellar signs, the cerebral cortex showed an intense neuronal degeneration in the third layer without any glial proliferation. Buchanan, Overholt, and Neubuerger[33] reported a case in association with Pick's disease. However, at autopsy a carcinoma of the bronchus was found, and it is possible that this was of etiologic significance. The present cases confirm the findings of others, namely, loss of neurons in the third and fifth cortical layers.

The striking parkinsonian immobility and rigidity which were observed in the late stages of the disease are more commonly found in the sporadic olivopontocerebellar degenerations than in the familial cerebello-olivary. That it may occur in the latter disease is attested by the reports of Welte[34] and Rosenhagen.[35] The site of the lesions responsible for the development of this type of rigidity has been much debated. Aring[36] found cavitation in the corpus striatum, while Rosenhagen associated the parkinsonian features with lesions in the substantia nigra. This is in keeping with Greenfield and Bosanquet's[37] findings of brainstem lesions in parkinsonism. They concluded that lesions in the basal ganglia in paralysis agitans were slight by comparison with those in the brainstem and did not differ essentially from those found in normal senile brains, whereas there were definite lesions in the substantia nigra.

In the case above, gross generalized rigidity was associated with marked loss of pigmented cells in the substantia nigra, and it appeared to be significant.

The cause of these systematized degenerations of the nervous system remains largely unknown. For the moment, ignorance is conveniently cloaked by the postulate of abiotrophy, "a degeneration or decay in consequence of a defect of vital endurance."[38]

SUMMARY

A family is described in which several members developed a profound disturbance of stance and equilibration followed by progressive rigidity and dementia. The father apparently transmitted this disease, since he developed a similar condition at the age of 44. Postmortem examination showed profound cerebellar atrophy with degeneration in the olivary nuclei and substantia nigra. The interrelationships of the cerebellar degenerations are discussed.

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CLINICAL PATHOLOGIC CONFERENCE

E. P. Richardson, Jr., M.D. Section Editor

Presented by *Charles Rupp, M.D. and Helena E. Riggs, M.D.*

A 55 year old white man was hospitalized September 14, 1950 because of headache and personality change. Four months earlier the patient complained of severe headache and poor vision. His local physician told him that he had high blood pressure. During the ensuing three months he developed a staggering gait and tremor of the upper extremities. Two weeks before admission he began to have urinary incontinence. His family noticed marked personality changes. He was careless about his cleanliness, lost interest in his work, talked loudly, and was noisy. He lost 25 pounds in weight, but there was no vomiting.

The admission examination showed a well-developed but emaciated man. Temperature was 98° F., pulse 90, and respirations 20. Blood pressure was 230/150. Physical examination was negative except for enlargement of the heart to the left. The liver could not be palpated, nor was there any peripheral edema.

On neurologic examination the patient was cooperative but was confused and showed loss of both recent and remote memory. His speech was slightly dysarthric, and occasionally he exhibited explosive laughter without provocation. The cranial nerve examination was negative except that the eye grounds showed hypertensive retinopathy with hemorrhages, exudates, and early edema of disks, and there was a tremor of the tongue. All of the deep reflexes were increased. There was bilateral ankle clonus. Plantar responses were normal. Hoffmann's sign was positive on the right. There was an intention tremor of both upper extremities, and tremor was also present at rest. The patient walked with a staggering gait, and the Romberg sign was positive.

Laboratory studies showed a hemoglobin of 11.2 gm., red cell count 3,100,000, white cell count 14,000, with 80 per cent polymorphonuclear cells and 20 per cent lymphocytes. Fasting blood sugar was 132 mg. per cent, blood urea nitrogen 48 mg. per cent. Blood serology was negative. Urinalysis revealed 4+ albumin with occasional hyaline and granular casts.

A chest film showed a moderate degree of emphysema with some cardiac enlargement. The skull film was negative.

Spinal puncture revealed an initial pressure of 260 mm. The fluid was clear and colorless. There were no cells. The protein was 200 mg. per cent, sugar 65 mg. per cent, serology negative, and colloidal gold, 00122210000.

During the first week in the hospital, the patient developed slight left-sided weakness with a positive Babinski sign. There was an inconstant Babinski on the right. Proprioceptive sense was diminished in the legs, and some degree of astereognosis was present in both hands. Pain appreciation was definitely diminished over the entire left side. His mental condition deteriorated. He exhibited marked euphoria. Following a spinal puncture on September 27, 1950, the patient immediately became cyanotic and developed Cheyne-Stokes respirations. His pulse became irregular, his right pupil dilated, and he sank into a deep coma. Death occurred within an hour.

DISCUSSION

DR. CHARLES RUPP: This patient complained of headache and poor vision, and then over a four-month period rapidly de-

From the Philadelphia General Hospital, Philadelphia, Pennsylvania.

veloped signs of diffuse intracranial involvement with cerebellar, bilateral pyramidal tract, and sensory signs, along with mental changes. In addition, he had some degree of increased intracranial pressure, as manifested by the spinal fluid pressure of 260 mm. The rather rapid exitus after the final lumbar puncture indicates that death resulted from acute medullary compression. He had marked hypertension, cardiac enlargement, hypertensive retinal changes, the blood urea nitrogen was elevated, and urinalysis was compatible with nephritic involvement. The clinical findings can, therefore, be explained on the basis of a severe hypertensive encephalopathy, brain edema, increased intracranial pressure, and, quite likely, multiple areas of encephalomalacia.

The fairly severe anemia and 25-pound weight loss suggest the possibility of a malignancy with multiple intracranial metastases. Neurologic manifestations due to intracranial metastases may antedate symptoms referable to the primary tumor, but in this case, with evidence of widespread neurologic involvement, it would be reasonable to expect that the primary neoplasm would have attracted attention. However, particularly with carcinomas of the lung and occasionally of the kidney, the primary tumor is cryptic and is found only at necropsy. Were multiple metastases the cause of his illness, we would expect the eyegrounds to show a picture of true papilledema rather than that of a hypertensive retinopathy. The anemia and the weight loss are not uncommon in severe hypertention with malignant nephrosclerosis.

STUDENT: I am not clear as to what you mean by hypertensive encephalopathy.

DR. RUPP: Frequently the term is applied loosely as a diagnostic label for any cerebral symptoms, such as headaches, vertigo, and convulsions, which may occur in a patient with hypertension. More specifically, hypertensive encephalopathy is a cerebral disorder associated with malignant hypertension and usually renal disturbances, such as nephritis or nephrosclerosis. The onset is usually abrupt or subacute, and the disorder is characterized by headaches and visual disturbances. Often there are convulsions, disturbances in consciousness, confusion, vomiting, and focal neurologic signs, such as aphasia or hemiplegia. The spinal fluid pressure is usually elevated and the spinal fluid protein content increased. The eyegrounds generally show some swelling of the disks, hemorrhages, and exudates. In some cases the symptoms may remit. In others, as in this case, the course is progressive until death ensues. Dr. Riggs will say something regarding the pathologic findings.

DR. FAUST (Resident): The confusion, personality changes, and euphoria suggest frontal lobe involvement. He also had cerebellar symptoms. Is it not true that cerebellar symptoms sometime occur in cases with frontal lobe tumors? Could the clinical picture be explained on the basis of a rapidly growing frontal lobe tumor, such as a spongioblastoma?

DR. RUPP: Cerebellar symptoms, particularly ataxia, do occur in some cases with frontal lobe neoplasms and may be confusing. Some who have written on this topic give the impression that, aside from ataxia, other cerebellar symptoms are slight or inconspicuous when the cerebellar signs are due to frontal lobe involvement. Others equally eminent and experienced state that all of the symptoms usually referable to the cerebellum, such as intention tremor, dysdiadokinesia, and nystagmus, are to be found. Personally, I am unaware of any clearcut means of differentiation. Associated symptoms may at times be helpful, but in some cases one must resort to ventriculography for the final answer. In this case there was a variety of marked cerebellar symptoms, not just ataxia. Dr. Faust's point is well taken, but the symptoms are rather diffuse to be accounted for on the basis of a frontal glioma alone. Also, if one were to accept his explanation, one would be forced to regard all the evidence of malignant hypertension as purely coincidental. This is difficult to do since it is so overwhelming.

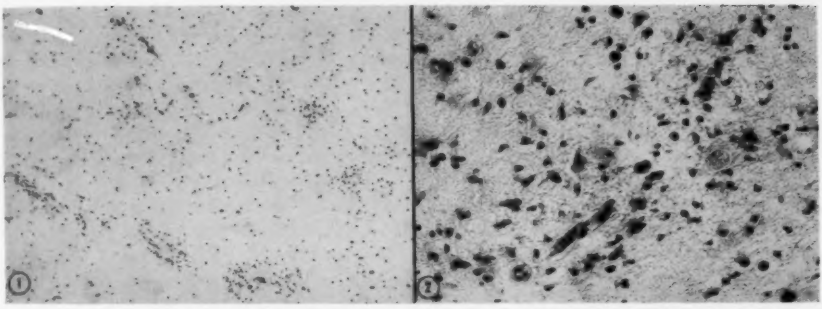

FIG. 1. Appearance of typical foci in brachium pontis. Small aggregations of microglia and astrocytes located in relation to blood vessels (low power).
FIG. 2. High power of one of the foci. Capillaries show endothelial swelling and proliferation. Myelin is destroyed in these areas, but the lesion has not progressed to complete tissue necrosis.

DR. FAUST: What is the mechanism responsible for the appearance of cerebellar signs associated with frontal lobe lesions?

DR. RUPP: There are several theories. One is that there is some interference with the frontopontocerebellar circuits. Another is that with increased intracranial pressure there is a tamponading of the cerebellum against the bony structures of the posterior fossa. Cerebellar signs, however, may occur in frontal lesions not accompanied by increased intracranial pressure.

DR. HARPRING (Resident): How do you explain his sensory symptoms?

DR. RUPP: This patient's blunted sensorium makes any evaluation of sensation difficult. Pain perception was definitely diminished over the entire left side. There was also a slight but definite left-sided weakness. A lesion in the posterior part of the internal capsule could explain this finding. It is not clear just what is meant by some degree of astereognosis present in both hands. The description is very nonspecific. One does not know whether he misidentified some objects because of confusion or lack of attention. With widespread cerebral involvement, there might also be some parietal lobe dysfunction. Again the statement that proprioceptive sense was diminished in the legs is vague. It is well known that vibratory sense is diminished to absent in the legs of elderly patients. Position sense is rarely impaired.

STUDENT: Could a degenerative process such as multiple sclerosis be the cause?

DR. RUPP: Against the diagnosis of multiple sclerosis are the age of the patient, the rapidly progressive downhill course, the history of headaches, the hypertensive retinopathy with swollen disks, increased intracranial pressure, and the associated vascular hypertension and nephritis.

PATHOLOGIC DISCUSSION

DR. HELENA E. RIGGS: Dr. Rupp has correctly interpreted the neurologic findings as a phase of a generalized systemic disorder. This case is an instance of malignant nephrosclerosis in which the cerebral manifestations overshadowed the somatic symptomatology. Parenthetically, we might remark that the case demonstrated the necessity of evaluating neurologic dysfunction in the light of the total clinical picture. At necropsy the patient was found to have a heart weighing 450 gm. with concentric hypertrophy of the left ventricle. The aorta and coronary arteries showed relatively little atherosclerosis, but the kidney, adrenals, and pancreas were the sites of extensive necrotizing arteritis. Similar vascular changes were present in the small arteries of the subarachnoid space and the intrinsic ves-

sels of the brain.

Presumably the onset of neurologic disability with headache and failing vision marked the onset of the malignant phase of hypertension in this individual. By the time of admission the condition was well established, with some degree of renal insufficiency and widespread damage in the central nervous system.

Surprisingly, the brain showed no focal lesions on gross examination and the ventricular system was not dilated. The specimen was large and heavy (1,450 gm.) and cut with increased resistance. The convolutions were flattened and the brainstem was markedly swollen. The uncus was deeply grooved on both sides and the cerebellar tonsils prolapsed and compressed against the medulla. The degree of brain swelling probably explains the unfavorable reaction to lumbar puncture and the terminal development of a midbrain syndrome. The genesis of the patient's focal symptoms was revealed on histologic study. Numerous microscopic areas of degeneration were present in the cerebrum, cerebellum, and brainstem, involving both gray and white matter. These consisted of collections of microglial cells and fibrous astrocytes centering around small arteries and arterioles which were undergoing thrombosis or necrosis of their walls. None of the foci had progressed to complete tissue necrosis. The localization of these lesions provided an adequate explanation of the patient's neurologic syndrome. Involvement of the motor pathway occurred in the cerebral peduncle, the pyramid, and the lateral corticospinal tracts of the cervical cord. Cerebellar symptoms could be correlated with the presence of degenerative foci in the brachium pontis, the pontile nuclei, and the inferior olive, as well as occasional lesions in the medullary substance of the cerebellar hemispheres. In the medulla, the spinal lemniscus of one side was partially destroyed, and both gracile nuclei were the site of extensive microglial and astrocytic proliferation.

In view of the degree of psychic disturbance in this patient, it was surprising to find relatively few focal lesions in the cerebral white matter and none in the cortex. However, the cerebral cortex showed many areas where disturbance in architecture has resulted from neuronal loss and neuronophagia and satellitosis by oligoglia. The amygdaloid nucleus on one side was largely replaced by astrocytic and microglial cells.

■ We now come to the question, What is the origin of the cervical sympathetic nerve? That most ingenious physiologist, Dr. Augustus Waller, has made experiments, with Prof. J. Budge, which seem to prove that the nerve-fibres of the cervical sympathetic that go to the iris originate from the spinal cord, between the sixth cervical and the fourth dorsal vertebrae. We have ascertained that the origins of the fibres of the sympathetic going to the iris are more extended than they thought. A section of a lateral half of the spinal cord at the level of the fifth, the sixth, and even sometimes as low down as the ninth or tenth, dorsal vertebrae, affect the iris like the section of the sympathtic, though in a less degree. On the other hand, we have seen, as Schiff also has, that some of the fibres animating the iris ascend the cervical part of the spinal cord, and most probably go up to the medulla oblongata.

C. E. Brown-Séquard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

CASE REPORT

Subdural Abscess with Retinal Thrombophlebitis

James Stephens, M.R.C.P. and Keasley Welch, M.D.

THE CLINICAL PICTURE of cortical thrombophlebitis associated with pus in the subdural space has been established by Kubik and Adams[1] and by Schiller, Cairns, and Russell.[2] Usually secondary to infection of the paranasal sinuses, the symptoms are those of an acute, superficial hemispheral disturbance. The following case is reported because of the interesting retinal changes which occurred following evacuation of a subdural abscess.

CASE REPORT

A 14 year old school girl was admitted to the Denver General Hospital on May 29, 1954, with the complaints of headache and vomiting for seven days, stiffness of the neck for two days, and involuntary movements with weakness of the left leg for one day. Her temperature was 37.6° C., the pulse rate 64 per minute. There was bilateral papilledema of moderate degree, with considerable venous distention, and one small hemorrhage on the temporal side of the right disk. The external ocular movements were full, there was no diplopia, but to confrontation she showed a left homonymous hemianopsia. The rest of the cranial nerves were intact, except for a left central facial weakness. There was a left flaccid hemiparesis, most severe in the leg. The reflexes were generally diminished on the left and the plantar response extensor. Sense of passive movement was impaired at the left great toe. Several times during the examination, focal motor seizures occurred in the left foot, lasting one-half to one minute and never becoming generalized. There was considerable resistance to passive flexion of the neck. The general physical examination was negative. A diagnosis of cortical thrombophlebitis was made.

The spinal fluid contained 56 cells, of which 42 were polymorphonuclear cells and 14 lymphocytes. The sugar was 70 mg. per 100 cc., the protein 80 mg. The total white count in the blood was 25,600, of which 84 per cent were of the polymorphonuclear series.

During the next 48 hours she was treated intensively with penicillin and streptomycin. Because of failure to respond and the likelihood of a coexistent subdural abscess, operation was undertaken on May 31, 1954. Burr holes were made in the midfrontal area, behind the ear, and in the posterior parietooccipital area. Incision of the dura yielded clear cerebrospinal fluid from all areas, and the cortical veins were not obviously thrombosed. On probing through the posterior burr hole, pus was encountered adjacent to the falx and about 30 cc. of fluid were removed. Alpha hemolytic *Streptococci* grew on culture.

The day after operation almost complete external ophthalmoplegia was noted. The papilledema had increased, and there were several new hemorrhages. The retinal veins were grossly dilated and segmental occlusions were seen in at least four areas. The subdural abscess required tapping on one further occasion, and air injected at this time was shown radiologically to be freely mobile along the falx, con-

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firming the situation of the abscess. Since films of the paranasal sinuses showed pansinusitis (left frontal, ethmoid, maxillary), a subturbinate ethmoidectomy and transnasal left antrostomy were performed. Her subsequent course was one of steady improvement, and within two months she had become symptom-free and demonstrated no abnormal physical signs.

DISCUSSION

Although venous thromboses of the retina are not infrequent, particularly among the elderly, and may be recurrent, their association with cortical thrombophlebitis is an extremely rare one. In this case the segmental occlusions were noted at the same time as the development of presumptive cavernous sinus thrombosis, and it would be reasonable to postulate retrograde spread along the central veins of the retinas. The association with infections is established, and Bender[3] reported a case of bilateral retinal venous and arterial thromboses following the removal of septic teeth. Goh in 1897[4] reported a case of bilateral venous thrombosis associated with gangrenous stomatitis and septicemia, while Greenwood[5] cultured *Streptococci* from the blood in a similar case. This is the organism usually found in cases of subdural abscess secondary to infection of the paranasal sinuses. Schiller and co-workers commented that it is "remarkable that a relatively thin film of pus in the subdural space can produce such complete hemiplegia. Blood accumulating in the subdural space at the same rate does not produce the same degree of paralysis, if indeed it produces any."[2]

It is clear in the case described above, where subdural pus was localized adjacent to the posterior part of the falx, that the initial symptoms were produced by thrombosis of cortical veins. The subsequent evidence of spread to basal sinuses and retinal veins supports this contention.

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CONFERENCE

on

TRAINING in CLINICAL NEUROLOGY

Under the Auspices of the

NATIONAL ADVISORY NEUROLOGICAL DISEASES AND BLINDNESS COUNCIL

of the

NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND BLINDNESS

NATIONAL INSTITUTES OF HEALTH

Bethesda, Maryland

Held April 23, 1956 at the Jefferson Hotel, St. Louis, Missouri

Introductory Comments

A. B. Baker, M.D.

IT IS MY PRIVILEGE to welcome you to this first conference on neurologic education held by the United States Public Health Service. I sincerely hope it will be a profitable and constructive meeting.

A little over three years ago, when a number of us were invited to participate in the activities of the training grant program of the National Institute of Neurological Diseases and Blindness, we readily accepted, knowing the acute needs in this field and feeling that here was a place where a real contribution could be made. We were all well aware of the large component of medical practice that consisted of neurologic problems and the need for intensified training of the graduating physician to handle these problems. We were also well aware of the rapidly increasing scope of the neurology field in both its basic and clinical phases and therefore the need for specially trained personnel to carry out neurologic education. Finally we realized that there was a tremendous shortage of teachers and researchers in the field of neurology which, if not remedied, would impede any rapid expansion in training, research, and service in this field. Knowing these problems, we on the first Neurology Training Grant Committee realized that we were faced with a real job that would take a great deal of time and effort and might be tainted with some disappointments and frustrations.

Actually, all of us who first embarked upon this work were amazed by the enthusiastic reception of this training program by neurologic educators, deans, and by the National Congress. We had felt originally that this program would develop slowly, giving us ample opportunity to follow its course carefully and evaluate progress. This has not been possible. The enthusiastic reception of this program by medical schools and hospitals immediately placed tremendous demands upon our committee for more intense activity in the proper administration of the program. The most understanding attitude of Congress made available the funds necessary to support this training program to its fullest extent. I believe a special vote of thanks is due Dr. Pearce Bailey and also the

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members of the National Committee for Research in Neurological Disorders for the excellent job they have done in interpreting the needs of this training program to Congress and gaining its support. Obviously, without appropriate financing, this training program would have been severely limited.

The Neurology Training Grant Committee readily accepted the challenge of this rapidly expanding program and has worked very hard to make it a success. Its efforts during the past three years have culminated in this conference. It was felt by the committee and by the National Advisory Neurological Diseases and Blindness Council that such a conference held at this time might aid the program in many ways. It could serve to bring together the many program directors so that they would have an opportunity to discuss mutual problems involved in neurologic education. Such an exchange of ideas is always healthy and fruitful. It would enable potential program directors in such schools that as yet have no active program to obtain information regarding the help available and the problems involved in the instituting of a neurologic training program. Finally, such a conference would enable us to present to many of the deans of our medical schools the present needs in the field of neurology and neurologic education and the accomplishments of the program to date. I am sure all of us in the field of neurologic education realize that, without the understanding and cooperation of our deans, little can be accomplished in the furthering of our training in neurology in the medical schools.

Needs in Neurology

Pearce Bailey, M.D.

THE PROBLEM which I have been asked to introduce is needs in neurology, particularly in clinical neurology today. This is a complex problem because the identity of clinical neurology in the general field of medicine has been a moot question, ever since its colorful inception by S. Weir Mitchell and William A. Hammond at the end of the Civil War.

In view of the complexity of the problem, I shall touch upon it only in the light of certain new developments which have taken place in the field of neurology during the past ten years—developments which demonstrate the primary importance of neurologic and sensory disorders to health and disease. Further elucidation of the needs in neurology is, of course, an objective of this conference and undoubtedly will come as the discussions proceed.

More than two decades ago, at the First International Neurological Congress in Berne, Switzerland, a famous New York neurologist, Bernard Sachs, called the nervous system the master tissue of the body and suggested it be treated as a focal point in medical teaching and research. "Neurology," he said, "is the fundamental specialty of medical art."

Only a few years ago, the famous professor of neurology at the University of Oslo, G. Monrad-Krohn, wrote to the effect that the nervous system is the central organ of the body, centrally situated and central to all bodily functions. He mentioned, therefore, that it should occupy a central position in medical education.

These statements by Sachs and Monrad-Krohn about the importance of the nervous system to medicine, and, indeed, similar allegations by many other distinguished authorities, have never been disputed in open forum, as far as I know. Equally undisputed is the belief that training programs in clinical neurology have not yet charted an even and enduring course in medical education; nor have they, to this time, achieved a significance commensurate with the importance ascribed to the nervous system by Monrad-Krohn, Sachs, and many others.

Let us assume for the moment that these assumptions of Sachs and Monrad-Krohn are correct and consider some of

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the new developments in neurology and the studies on its status and needs during the last ten years.

In 1946, after serving as a neurologist in the Navy during World War II, I accepted the responsibility of organizing a neurology service for the first time in the medical department of the Veterans Administration. It was then that I was first struck by the paucity of qualified teachers and training facilities in clinical neurology in large sections of the country and by the lack of finances to provide them. It was at this time, too, that I became acutely aware of neurology's lack of constructive liaison with other medical disciplines in many medical schools and of the dangerously dwindling numbers of young men interested in entering neurologic training. I believe it was in this year, 1946, that clinical neurology in the United States reached an all time low in attracting promising young men to its ranks.

Nonetheless, the Veterans Administration neurology program did "get off the ground" and expanded even in this apparently chilly climate. About 40 neurologic residency services were established under Veterans Administration auspices, most of them affiliated with teaching hospitals in medical schools. The growth of the program, however, was greatly aided by other new developments with which its destiny became closely interlocked: the organization in 1948 of the American Academy of Neurology by A. B. Baker and others; the creation of an official journal, *Neurology*, under the editorship of Russell N. DeJong; and the increasing public attention which began to be focused on chronic neurologic disorders because of the modern rehabilitation movement.

While these new developments in neurology were gaining momentum, the problem of its status and needs became a favorite topic for presidential addresses before national neurologic societies. Between 1946 and 1950, the status and needs of neurology provided the central theme of at least six presidential addresses before national neurologic societies, including the Section on Nervous and Mental Diseases of the American Medical Association. Another paper by Russell N. DeJong was discussed by Roland P. Mackay and myself before the Association of American Medical Colleges at Lake Placid in 1950. In addition, the problem of the needs in neurology was made the subject of an extensive survey and report in 1949 by the Pollock committee of the American Neurological Association. Later in that year, this was discussed by Monrad-Krohn, Foster Kennedy, and others during the executive sessions of the Fourth International Neurological Congress held in Paris. The essence of the Pollock committee report was the lack of training and research facilities in neurology and the lack of trained physicians to serve as teachers and to care for the vast number of neurologic patients in this country. Some of the highlights of the Pollock report were: 1) less than 20 per cent of the country's medical schools had adequate training programs in neurology; 2) the chairman of the department or division of neurology in most medical schools was not a qualified neurologist; 3) there was no uniformity in the organization or teaching of neurology throughout the country; 4) there was a proportional disparity in various sections of the United States, of the number of qualified neurologists to practicing physicians, for example, in Northeast 1 to 423, Midwest 1 to 668, Pacific

1 to 814, Southeast 1-1 to 783, Mountain 1-2 to 614, Southwest 1-4 to 547; in about six states there was not a single qualified neurologist; and 5) the bulk of neurologic patients, about 90 per cent, were never seen by a qualified neurologist.

These presidential addresses and committee reports on the status and needs of neurology, though they often bemoaned the current plight of neurology, nearly all analyzed the needs and advocated means for a better future. Among them were recommendations for 1) additional funds for the support of neurologic training and research; 2) formulation of an appropriate public relations program in neurology; 3) more curriculum hours for neurology in undergraduate medical education; 4) more autonomy, both professional and budgetary, for neurology in the organizational structures of medical schools; 5) development of a more therapeutic orientation in neurologists under training; and 6) preventive measures against further splintering of neurology into other disciplines.

Provocative as these addresses may have been, their influence on medical thinking undoubtedly was quite limited. The audiences in all instances except one were made up of neurologists, thereby giving to the sessions a parochial note of only convincing further those already convinced. The one exception was the Lake Placid meeting before a group of medical school deans, but here the speaker and the discussants were almost talking to themselves, for there were not over a dozen people in the audience.

However, these group presentations and discussions and the new activities in neurology from 1946 to 1950, already mentioned, while they did not provide sufficient fuel for a true renaissance of clinical neurology, did supply new opportunities for training neurologists. They also induced neurologists to focus more sharply on the depth of the problem. But new opportunities and sharp thinking do not necessarily arouse new incentives, especially when they do not contain all the ingredients essential to invigorate a static problem in an unfavorable setting. Thus, in spite of their zeal, they did not supply badly needed items such as stipends for neurologists-in-training and grants for training programs in medical schools. At the same time, the growing medical manpower shortage, from which a rejuvenated neurology would have to draw, had become even more acute because of the Korean War.

There was some reassurance, however, for these anxieties which reached a peak in 1950. The reassurance came from two new quarters: first, from an increasing public awareness of the impact of neurologic disorders as a public health problem, which was aroused by the organization of several voluntary health agencies dedicated to the welfare of certain groups of neurologic disabilities, particularly cerebral palsy, multiple sclerosis, muscular dystrophy, and epilepsy; second, from the phenomenal growth since World War II of experimental neurology which had reached a stature worthy of categorical consideration.

The growth of voluntary agencies dedicated to neurologic diseases and the rise of experimental neurology seemed to converge at a point in soil which already had been tilled by the new movements in clinical neurology for an amalgamation of efforts in behalf of neurologic patients. The spontaneous confluence of these three forces, the voluntary agencies, experimental neurology, and the new activities in clinical neurology,

somehow led to the creation and activation of the National Institute of Neurological Diseases and Blindness in 1951. As some of you know, those of you who participated in the program of the institute, the first two years of its existence were an intense struggle for the initiation of a program just on a planning basis. During these first two years, the institute struggled along on a small, static budget, but finally in 1953 the ring of inertia was broken and henceforth its program has developed into a dynamic and productive operation. In 1951 and 1952 the institute's annual appropriation hovered around the million dollar mark; in 1953 it was increased to 4.5 million; and the House of Representatives allowance for the coming year is over 14 million.

The part of the institute's program which concerns us most today is its grants program in graduate training to develop clinical teachers and investigators in neurologic and sensory disorders. This part of the program, incidentally, was the hardest one of all for which to obtain financial and moral support, even though it is the segment of the program most intimately related to the needs of neurology.

I shall not burden you further with a recount of the development of the institute's national program in graduate neurologic education. Recently this has been summarized in a special issue of the Newsletter contained in the journal, *Neurology* (Vol. 5, No. 12, December 1955).

To return to the needs in neurology, it is my belief that some of those expressed in the presidential addresses and committee reports referred to previously have been, at least partially, satisfied as a result of the changing scene in clinical and experimental neurology, the rise of voluntary health organizations, and the promulgation of the institute's national program. Funds for the initiation or strengthening of existing training programs are now available. The position of neurology in medical public relations has improved in recent years, and the tendency for neurology to continually splinter itself has been diminished, especially since the formation of the National Committee for Research in Neurological Disorders in 1952.

The problem of cultivating a more therapeutic orientation in the training of young neurologists will still remain until all training centers give the neurologic resident full therapeutic responsibility for neurologic patients he sees on the hospital ward. This is not an easy task, for clinical neurology always has been firmly rooted in morphology and has placed a premium on point-to-point clinicoanatomic correlations.

There is a certain fascination, as we all know, in vibrant discussion on the problem of clinicoanatomic correlations for which the nervous system supplies such an ideal substrate. But this can be overdone, becoming a sort of indoor sport for which the neurologist and the neurologic patient eventually pay the bill in terms of wasted time or increased suffering. For a national program to survive today, its central core must be anchored firmly to the welfare of the patient. In terms of modern medical thinking, I do not believe a purely diagnostic specialty can survive.

In closing, permit me to stress the great need in clinical neurology today to expand the scope of its interests. Neurology always has been stalked by a danger of being compressed into a narrow groove. As far back as 1913,

Dana sounded a warning of this impending danger when he wrote, "The neurologist must expand his interest or sink into the narrow niche of curator of the scleroses or an appraiser of teratological defects."

It seems that in the past an undue preoccupation on the part of clinical neurologists with psychiatry, and more recently with neurologic surgery, unfortunately has thinned their lines of communication with internal medicine, to which they were firmly anchored when it began as a specialty after the Civil War. What is equally as unfortunate is the fact that a liaison of neurology with pediatrics is for all practical purposes almost nonexistent, even though a large proportion of neurologic patients are children. The institute is now planning training programs in developmental pediatric neurology as part of a collaborative research program in cerebral palsy, which should alleviate this situation by placing neurologists in intimate contact not only with pediatricians but also with obstetricians, with infants as well as children.

The tendency of neurology in the past to narrow its sphere of activity from a clinical standpoint has also obtained to a certain degree in research activities. In the beginning, neurology, following its original morphologic orientation, aligned itself almost exclusively to neuropathology. But when medical research took a more functional turn at the beginning of the twentieth century, neurology veered toward neurophysiology, especially electrophysiology, where today the maximum research activities are concentrated. It is hoped, however, that all activities of neurologists will not be devoted exclusively to this field, important as it is, but that they will enter aggressively the promising new fields of electron microscopy, tissue culture, and biochemistry. It might be well to encourage, wherever possible, the development of these technics in the basic science aspects of the neurologic training program.

If neurologists can expand their interests along these lines, both clinically and in the laboratory, the remaining needs in neurology for additional curriculum hours in undergraduate education and more professional and budgetary autonomy will be resolved.

It also might well introduce an era where the recognition of the importance of the nervous system and neurology, recommended by Bernard Sachs and Monrad-Krohn, will be fulfilled.

Discussion of Dr. Bailey's Paper

H. Houston Merritt, M.D.

WHAT I HAVE TO SAY will be mainly in the sense of reinforcement of Dr. Bailey's paper. This conference has resulted from the efforts of a great many people and I should like to pay tribute to them at this time. This meeting could not have happened if we had not had a man to head the National Institute of Neurological Diseases and Blindness with the energy and vision that Dr. Bailey has had. Contributing also to this occasion was the National Committee for Research in Nervous Diseases, headed by Dr. Baker, and I believe supported by Doctors Traeger, Stone, and Brooks and others in the voluntary health groups. Also, the revival of interest in neurology can be traced to the establishment and growth of the American Academy of Neurology. These three developments, I am sure, bode well for the future of neurology in the United States and in the world.

One of the most important problems facing us today is the training of teachers and leaders in the field of neurology. These teachers and leaders must be trained not only in the clinical fields, but also in the basic sciences. If we can successfully train our neurologists in the basic sciences, I am sure the role of neurology in the medical schools and academic councils is assured.

Now to reemphasize some points Dr. Bailey has raised. He stated that our relationships with psychiatry and neurosurgery are traditional. These, of course, should be kept at a high level and improved. It is even more important, however, that we infiltrate the services of medicine and pediatrics. It is only through contact with these two services that we can further expand our specialty. Dr. Bailey emphasized the fact that neurology has been too much a diagnostic specialty. It is important to point out that the diagnostic phase of neurology is only a preliminary and not the end. The real goal is the care and cure of the patient. Neurology, therefore, must be directed toward therapeutic lines, and residents must be trained to assume therapeutic responsibility. Although the direction of neurologic research in the past has been toward neuropathology, neuroanatomy, and neurophysiology, it is time now to turn our attention also to biochemistry, endocrinology, and nutrition (particularly vitamins), because only through these are we going to determine the causes of many of the diseases of the nervous system and find new forms of therapy.

I would like to conclude by saying that I am happy to be here both as a representative of the National Advisory Neurological Diseases and Blindness Council and a participant in the training program. This signal occasion is a happy omen for the future.

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Accomplishments of the Graduate Training Grant Program in Clinical Neurology

Russell N. DeJong, M.D.

THE SUBJECT "Accomplishments of the Graduate Training Grant Program in Clinical Neurology" is one that can be discussed in a variety of ways. Each of these, however, has as its objective the attempt to assess the individual training programs, in order to discover what progress has been made in the graduate teaching of neurology under grants from the National Institute of Neurological Diseases and Blindness. It must be borne in mind, of course, that the Graduate Training Grant Program was started less than three years ago, and many programs have been active for even shorter periods of time. This report, therefore, must be considered as a very preliminary one, but it does show, I believe, that a great deal has been accomplished even in this brief span of years.

First, one can take a statistical approach and recount exactly what appears to have been accomplished through the training grant program. It will be obvious, however, that statistics do not necessarily give an accurate record of what has actually been accomplished. In the second place, one can speak in generalities tinged with hope and optimism and try to present statements that indicate that the results thus far fall in very closely with Dr. Bailey's recent account of the needs in the field of neurology. Thirdly, I can discuss the subject from a personal point of view and state what our grant has helped us to accomplish locally at Michigan, and also mention some of the results at other training centers. It might be best more or less to compromise by trying to do each of these briefly.

First, I will give you a brief statistical analysis based on answers to a questionnaire sent by Dr. Gordon Seger to all neurology training grant program directors who have had a grant in clinical neurology for six months or more. These reports are very revealing and would certainly lend support to a very optimistic view of the program thus far. Before presenting the figures, however, it must be stated that they do not necessarily give an actual report of what has been accomplished. The directors were asked to name those who completed training under them since their programs started, regardless of the source of support of the individuals, and to name those now in residency. It must be borne in mind that some of the programs were

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very active even before grants were received, and many of the people who have completed their training were already in the programs prior to the institution of the grants and would probably have completed their training regardless of whether the program received additional support from the National Institute of Neurological Diseases and Blindness. Furthermore, many of these programs were already large ones with many residents and the addition of one or two more trainees would not appreciably change their quotas. On the other hand, some of the programs were inaugurated entirely through help from the National Institute of Neurological Diseases and Blindness, and there would have been no accomplishment whatever without this assistance. Lastly, I regret to say that, despite what Dr. Seger and the other members of the Neurology Training Grant Committee felt was a very clear and precise questionnaire, many of the program directors misinterpreted the questions and consequently it has been somewhat difficult to categorize accurately their reports. However, I shall try to summarize the statistical results of this questionnaire.

Information was requested from all program directors who have had grants for six months or more. This totaled 37 programs, and reports were received from all. It must be borne in mind, however, that only five of these were activated in 1953, 25 in 1954 (and I have not separated those activated in January from those started in July of 1954), and seven in 1955. In addition, some of the programs were unable to start work immediately upon receiving their grants. In fact, some of them have not yet been able to secure staff and become activated. Residents reported to have completed their training under these grants number 83. Of these, 16 have been certified by the American Board of Psychiatry and Neurology, 45 are reported as board eligible, and 36 now hold positions in training institutions as teachers or clinical investigators. In addition, 92 others not specializing in clinical neurology received six or more months of training under these programs. These 92 consisted of physicians interested primarily in neurosurgery, psychiatry, and internal medicine. I must state that in some of the programs the only residents listed were men in these other specialties. The total number of residents now in training (that is, residents serving on an annual basis and not those from other services who are spending one, two, or three months in neurology) is reported as 158. Of these, 129 are specializing in neurology and the remainder in a variety of fields, but again primarily in neurosurgery, psychiatry, and internal medicine. In almost every case the residents, especially those in the second and third years, are teaching medical students. In a few instances the teaching is in neuropathology, neuroanatomy, and neurophysiology, usually in addition to clinical neurology, but in most cases resident teaching is limited to the field of clinical neurology. Only 22 current vacancies are listed in the resident programs, with 13 vacancies for next July and five vacancies in Veterans Administration programs affiliated with a training grant program. Some centers are not yet approved for training and these, of course, can list no residency vacancies.

Program directors report that, since the start of these training grants, a total of 79 staff members have been added. The majority of these additional staff members are presumably clinical neu-

rologists, but some of them are listed as neurophysiologists, neuroanatomists, pharmacologists, and so on, and in quite a few instances the actual activity of the new staff members was not specified. A total of only 13 actual faculty vacancies is reported, but many directors made the statement that they would like to add to their staffs if funds or personnel were available.

It should be mentioned, and is of interest, that out of the 83 men and women who have completed their training in neurology since these programs started, 48 were trained in seven centers and 84 residents out of the 158 now in training are in these same seven centers. Thus it is seen that our statistics depend largely upon a very small group of programs, of which three were activated in 1953, two in January 1954, and two in July 1954. All but one, however, were already active programs before the grants were allocated.

Now I should like to generalize a little, which I feel that I am justified in doing on the basis of some experience on the Neurology Training Grant Committee and a very thorough review of the questionnaires. In applying for a grant, the director is asked to state whether he is establishing a new program, expanding an already active one, improving an already active one, or continuing the same program. The committee, in awarding grants, feels that it can be of a great deal of help in all four of these purposes. Grants have been given to many schools and hospitals where there was no active resident training program and a weak undergraduate teaching program, but where it was felt the director himself had ability and incentive and with encouragement and financial assistance he could build up an effective graduate program and at the same time improve the quality of the undergraduate teaching and stimulate neurology in general by inducing enthusiasm for the field to those still in their undergraduate years. Quite a few can be named where this has worked very well. Sometimes, because of geographic location of the school, financial difficulties within the center, or little interest in neurology in years past, the grant has aided in the development of an expanding department with a centrifugal spread of knowledge in and an interest for neurology to the contiguous areas.

In other places where there had long been an active program, but one that had labored under a somewhat meager budget (and all of us who are in medical school situations know how difficult it is to expand our budgets, especially since the neurology department is usually a small one and must compete with the larger services such as medicine and surgery), it has been possible to increase the value of the training program by bringing in additional personnel in the basic sciences, giving the residents more time and opportunity for investigative work during their training years, and in general increasing the educational value of the program. In this way an active program has been improved, and, furthermore, has often also been expanded by allowing the director to take on additional residents as well as additional faculty personnel. In some training centers neurology has been able to achieve some degree of autonomy in this way, and has developed from a sub-department or division into a service of its own where it is on a par with the other larger services. In this manner, too, programs which had originally had a one-year or

two-year approval by the American Medical Association and the American Board of Psychiatry and Neurology have been able to achieve a full three-year approval, so that the residents can get complete training in the center and then perhaps stay on in the vicinity in practice or in teaching. The accomplishments in expansion or improvement in the training programs is reflected in the large number of personnel that have been added in these 37 programs. It is true that the salaries of all of these individuals have not come from the training grants themselves, but in many centers the university or the hospital, seeing the expanding program, has augmented the institutional budget for the program simultaneously with the receipt of help from the National Institute of Neurological Diseases and Blindness.

Another very tangible evidence of the contribution of these programs has been the number of men who have gone into teaching and investigative work in neurology since their inauguration. Of the 83 men who have completed their work, 36 are now in teaching and investigational positions, and this percentage would obviously be larger if it were not for the fact that many individuals who have just completed their training are now in military service, while others are continuing their training on a higher level or in basic science work at other centers in this country or abroad prior to accepting teaching and research positions.

There are two more points that might be mentioned, although with some hesitation. In the first place, it is the major objective of the National Institute of Neurological Diseases and Blindness and of the men who have been on the Neurology Training Grant Committee to stimulate the training of teachers and clinical investigators in the field of neurologic disorders. Objection has frequently been raised to programs that largely train psychiatrists, neurosurgeons, and internists. It should be the major objective of our program to train neurologists, but I feel very strongly that we are accomplishing a great deal for medicine and for mankind if we aid in contributing good neurologic training to men in other fields. It is obvious that our programs should not be instituted mainly for the training of neurosurgeons, for instance, but if even a small percentage of our trainees are neurosurgeons and these neurosurgeons are trained to be good diagnosticians and neurologic clinicians, they will be much better neurosurgeons. Thus I think in all of our programs, we should feel that we can support neurosurgical trainees for periods of longer than six months and often a year or so, so that our surgical colleagues may go into practice and into teaching with a more sound neurologic background and perhaps some may be stimulated to embark on clinical investigation. And this applies to psychiatrists and internists, too. Unfortunately, there are many centers where the rift between neurology and psychiatry is becoming wider, and it is apparent from experiences on the American Board of Psychiatry and Neurology that many psychiatrists have an appallingly poor background knowledge of the structure and functions of the brain and nervous system. With the recent renaissance of interest in the organic background of the psychoses, from anatomic, physiologic, and pharmacologic points of view, it is up to us as neurologists to see that the future psychiatrists have a sound footing in neurology. Finally, while it is

trite to state that the best internists are those who have a broad concept of neurologic disease and of the neurologic manifestations and complications of systemic disease, it is obvious that those programs which train mainly internists, but internists with a good neurologic background, are making a real contribution too.

The other accomplishment to be mentioned with some reserve relates to finances. Through training grants, many of us have been able to increase the stipends for our residents. It has always bothered me that in my own institution, and in many others too, the residents, young men who have gone to college and medical school, have interned, and many of whom have married and have families, must start their residency at a salary far less than that paid the clerks and menial help in the hospital. Of course there is always a very good answer to this, and that is that these men are "in training;" "this is not a salary based on worth, but just a stipend given to a man who is still in school." There has been an increasing competition on a salary basis, with psychiatric residents in many places receiving salaries entirely out of range with those paid in other disciplines. And, of course, the Veterans Administration hospitals do pay a stipend slightly larger than that given in most teaching institutions. With the help of training grants, it has been possible to increase the stipends of many residents in training in neurology. Thus, these young men, who do have definite financial responsibilities and problems, are able to get at least a living wage while they are continuing their training in this specialty which all of us feel is of paramount importance in medicine. Thus it may be that certain good men, who because of other obligations might have had to shorten their period of training, go into other fields, or go to centers with inferior facilities, may be able to continue their careers and fit themselves for teaching and investigation.

Now I think that I should state just a little of what has been accomplished at Michigan, and our program is fortunate in being one of those that date back to 1953. Our development under this grant has been a gradual one, with, as has been the case in most other places, a little delay in the beginning. We did have a rather active program before we received our grant, and have always been fortunate, I believe, in having a rather generous budget from our medical school. Our program has always been one that has been oriented clinically to a major extent, although, of course, we feel that adequate emphasis must also be placed on both research and training in the basic sciences. With the financial assistance from this grant we have been able nearly to double the number of residents and fellows in training, as well as to increase our full-time faculty personnel. I believe that these residents are getting a better training now that they are available in larger numbers, because the work load is less and they have more time for individual work. Furthermore, the augmented staff is able to give more time to individual instruction, we have been able to assign longer periods for full-time work in the basic sciences and in ancillary fields such as physical medicine, and the residents have better facilities and more time for research and original investigation. Also, because the residents assist in undergraduate teaching, we have been able to give more individualized bedside instruction to our medical students. This

must be considered a very important part of our teaching programs, and one which all of us must bear in mind carefully; any program that tries to divorce undergraduate from graduate instruction is missing one of the major objectives of medical education.

I feel that the assistance we have received has been most valuable to us, and that its value will increase as time goes on. A review of other expanded programs shows a similar qualitative and quantitative expansion of training, with improvement in the caliber of the instruction and experience which parallels the increase in number of men in training. Many of the newly established programs are not able to list accomplishments to date, but, as many of these have had to "start from scratch" and have had difficulty in recruiting satisfactory personnel, their problems have been much more serious and in many cases it is too early for critical appraisal.

As a specific example of the effect that the training grant program has had in one center, I should like to quote to you, and to say that it incorporates my own feelings, the statement made by one of the program directors as his introduction to the answers on the questionnaire. "Let me say that I, as the program director, have greatly appreciated the help which the Institute has afforded us. Without it we could not carry out our program in neurology, and with it I feel that we have enhanced not only the program of neurology in our own state, but to a great extent throughout the neighboring states." I will add one more quotation from his letter, which I do not think applies in my own case but may in many others. "Curiously enough, since 1953 our own department has been under a solid footing here at our school of medicine and it is a great feeling personally to have it solidly accepted."

As was said earlier, sufficient time has hardly elapsed for a profound appraisal of the accomplishments to date in neurology of the Graduate Training Grant Program. I hope, however, that this brief account shows that much more has been done than might have been anticipated. Our results to date most certainly show that real and fundamental advances have been made, and there is every reason to believe that this is only the beginning, but one which foretells a most significant future.

Discussion of Dr. DeJong's Paper

Oliver H. Lowry, M.D.

IT IS DIFFICULT to discuss a paper when one wholeheartedly agrees with it. The encouragement of training clinical neurologists must also improve undergraduate training and training in peripheral related areas. No matter how specialized we become, medical training, both graduate and undergraduate, has to be taught as an integrated program. It is hard to divide the patient and separate the nervous system from the rest of the body.

I would like to discuss briefly the neurology training grant program as it affects our own school. I hope we fall into the category of having a good training program that has been made better. The main trouble with our program was that our staff was spread too thin to do a good teaching job. With the shortage of trained neurologists which exists everywhere, our clinical teaching load was especially heavy both for full time and part time personnel. At one time, undergraduate teaching alone consumed 750 hours per year for each of the full time staff and 150 hours a year for practicing neurologists who were assisting in the teaching responsibilities. As a result, the training of residents and interns suffered greatly and there was not sufficient time to devote to undergraduate students.

The training program of the National Institute of Neurologic Diseases and Blindness provided additional personnel and thus lightened the individual teaching load considerably. The undergraduate level of training in neurology was strengthened and, as a result, the number of senior students who elected neurology as a special study increased from a rare exception to ten or 12 a year out of a class of 85. Now the number of trained neurologists is increasing slowly but steadily, and each member of our full time staff has a minimum of two days per week for research activities. True, it is often difficult to appraise a new program accurately. Any improvement or change in teaching is hard to assess. I have the feeling, however, that you get good teaching when the teachers are enjoying what they are doing.

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Influence of Graduate Training Programs in Neurology on Undergraduate Medical Education

Francis M. Forster, M.D.

CONGRESS AUTHORIZED and then subsequently appropriated funds for this graduate training program in order to increase the number of physicians in the field of neurology. At first glance, therefore, it seems somewhat strange to have this particular title on the program, "Influence of Graduate Training Programs in Neurology on Undergraduate Medical Education." All of us in medical education learned long ago that it is not possible to make a sharp distinction between teaching, research, and service. There is so much overlap between the various areas that the presentation of a questionnaire regarding divisions between the three is strong indication of naivete on the part of the questioner. In the same way, it is not possible to distinguish clearly between graduate and undergraduate education, and, therefore, a graduate training program must, of necessity, have considerable influence on the associated undergraduate program. It is not possible to alter a graduate training program without exerting considerable influence on the associated undergraduate program.

The influence on the undergraduate program is manifold. The increase in teachers in the medical school due to this program provides more instruction for the undergraduate student. Initiation of new or augmentation of existing residency programs increases the number of physicians in the residency category who are in daily contact with the students. Moreover, whenever men are gathered together in a particular field, and if this is a viable, dynamic field such as neurology, inevitably research becomes an integral part of their thinking. These investigative thoughts become stimulating for the undergraduate student, either by direct contact with the research or by indirect contact due to the stimulation of the instructors. Therefore, the introduction of any program as large as this must undoubtedly have some impact on the undergraduate training program.

The first tangible evidence which one can look for in regard to the effect of this program would be the number of new faculty members. Twenty-eight of the training grants programs have increased their faculty by the use of funds from these grants. These 28 schools have added 80 faculty members in numbers from one to six per program, with an

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average of 2.5 new faculty members per training program. Under the stimulation of these 28 programs, there are 158 residents in medical neurology. This number does not include residents who are rotating through neurology from psychiatry, neurosurgery, internal medicine, or other services. These residents are training for the future teaching, investigation, and practice of neurology.

The graduate training program must, of necessity, have considerable impact on the clinical teaching of the undergraduate medical student. Through this grants program, some 80 faculty members have been added to the teaching programs and 158 residents have been added. This comprises a total of 238 additional teachers in the field of neurology. The residents play a very specific role in the teaching of clinical neurology. Any well planned program must have residents of different echelons, in addition to staff men at different echelons. In this way there is a pyramiding of responsibility and of teaching sophistication. This is of great importance. Questions which the young medical student fears might be too simple, he is far more apt to ask of the junior resident than he is of the senior resident or the staff men. Residents are in full time daily contact at the shoulder to shoulder level with the students and they are completely available at all times. One is almost tempted to say that the added number of residents is even more important than the added number of staff men, as far as the teaching of clinical neurology to the undergraduate student is concerned.

The role of teaching clinical neurology has a particularly pertinent impact on the total medical program. There is no other field of medicine so well adapted for the teaching of the art of medicine, both in dealing with the patient and the family. The young medical student assigned to neurology has a particularly good opportunity to learn the methodology of explaining, reassuring, and succoring the disabled patient, the chronically ill patient, and the incurable patient. This program, therefore, by placing more men in the teaching of neurology, strengthens the total aspect of medical education, one which has not received its proper stress.

One of the concerns of modern medical education is the paucity of men entering the preclinical sciences. This is especially true in anatomy and to a lesser extent in physiology. Nevertheless, this shortage of preclinical professors, which to all indications will become more acute in future years, has become a matter of concern for the administrations of many medical schools. One might well question then if this graduate training program had any impact on the undergraduate preclinical education. The answer to this is quite amazing. Of the 80 new faculty members added in the 28 schools, 50 of these members in 21 schools are actively engaged in teaching preclinical disciplines to medical students as well as residents. A few of these new faculty members are engaged in teaching biochemistry with special reference to the nervous system and a somewhat larger number are in physiology, but the overwhelming number are in the fields of neuroanatomy and neuropathology.

Moreover, the residents in training in neurology are also exerting an influence in the preclinical sciences. Twenty-seven of the residents are actively engaged in teaching neuroanatomy and 22 in the teaching of neuropathology to medical

students. These are second and third year residents in almost every instance, and are therefore not only mature, but also sophisticated in regard to the nervous system as well as to teaching. Only rarely is a first year resident encouraged or permitted to engage in the teaching of the undergraduate student. There is no resident engaged in teaching neurophysiology or neurochemistry to medical students. This is probably due to the complexities of these fields. The average resident is usually not qualified to teach in these two specific areas. This is most particularly true of neurochemistry, for it is a new science and is highly complex.

At first, this impact of the training program on undergraduate training, particularly in the preclinical years, might seem considerably surprising. However, to understand this well, it is important to understand the concepts of the new and dynamic neurology. Neurology as a specialty is in a progressive and vital phase. The old concept of a neuropsychiatrist is now no longer tenable. The teaching and indeed even the practice of both neurology and psychiatry by a single individual is looked upon with less favor now by most men engaged in the training of physicians in either of the two categories. The American Board of Psychiatry and Neurology has discouraged certification in both. While it is, of course, possible and permissible to be certified in both specialties, it is now so difficult and requires extra training that it is seldom a candidate is seen for examination in both subjects, especially simultaneously. The reasons for this are many. Probably the most important is that the present day neurologists have lost interest in the field of psychiatry, with its totally different concepts and methodologies. Modern neurology has developed into a scientifically and basically oriented subject. No department of neurology can exist and thrive as a department of clinical neurology. In order for a program really to be strong and to thrive, it is important that at least one, and preferably all, of the fundamental disciplines in neurology be represented in that department. These fundamental disciplines are neuroanatomy, neuropathology, neurophysiology, and neurochemistry. A department of clinical neurology devoid of contact with or orientation in research in any or all of these fields is a department in name only. Therefore, the departments of neurology, in order to recruit faculty members, must have outlets for them in the basic disciplines. This in itself is good, not only for neurology and medical research, but also for the medical schools as a whole. Clinicians with a basic interest when they engage in a teaching program of preclinical students have their teaching oriented basically from the neurologic standpoint, that is, all of the basic disciplines as well as the clinical discipline are considered and stress is placed in perspective to the clinical aspects. While in many programs the residents are not actively teaching in the field of neurophysiology, it is interesting to note that several program directors, when queried as to whether or not their residents taught neurophysiology, answered that they do not teach neurophysiology as a regular subject in the program, but they certainly teach clinical neurology with a neurophysiologic, neuroanatologic, and neuropathologic substrate. This is the new neurology which is not only developing and growing by its own right, but is liberally giving of its bounty to its colleagues, particularly in the preclinical sciences.

Discussion of Dr. Forster's Paper

Aura E. Severinghaus, Ph.D.

LADIES AND GENTLEMEN, I am indeed glad to be here and I have listened with interest and attention to Dr. Forster's excellent paper. I know I wasn't invited to stimulate my interest in neurology, for my interest has been obvious through most of my professional life. My research work kept me close to the nervous system. I have spent 20 years on the pituitary gland.

Of course, I feel very strongly that neurology has an important place in the undergraduate curriculum. It cuts across all of the disciplines, not only the clinical sciences but the basic sciences as well. Some ten years ago when we were reorganizing our own undergraduate curriculum, it was proposed time and time again that, because of our facilities, we should do more with neurology in the undergraduate curriculum. What has actually happened is all to the good. Although not a required clerkship, we have permitted our undergraduate students to elect work in neurology. They choose this field of their own accord because they are stimulated by what they find around them.

We are grateful that the National Advisory Neurological Diseases and Blindness Council has chosen to support training programs not only in schools where neurology might be encouraged to develop, but also in schools where neurology is already enthusiastically received, because both are rewarding. Our Neurological Institute has a rather imposing building of its own – something which immediately gives the undergraduate student the impression that neurology is important. Each year, when I talk to the second year students about planning their elective work for their third and fourth year programs, I point out that the discipline of neurology cuts across both the basic sciences and the clinical sciences. Even if I didn't talk in this way to the undergraduates, they would discover this fact on their own.

I am not here to admonish and instruct, but may I say that much depends on the relationship between departments and interdepartmental cooperation in the medical school itself. In our school, the neurologists have succeeded in establishing close liaison with other departments. In pediatric neurology, for example, 20 beds in the Babies Hospital are used for student instruction by residents and attending neurologists. Through such an integration of teaching, almost as many undergraduate beds are available in neurology at the medical school and Montefiore Hospital as we have in medicine. We have active research programs in neurophysiology and neuroanatomy which are housed in the medical school, attached to biochemistry, physiology, anatomy, and so on, and the researchers, although members of the department of neurology, are actually working in relation to physiology

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and anatomy. The neurology staff gives many lectures in the pharmacology course where there is an obvious close relation between the disciplines. In our first year, correlative clinics are held to show the student the importance of the basic sciences on disease entities. In the third year we have an elective program so that every student has at least three months of elective time which can be used in the clinic or in research. It turns out that on an elective basis about 70 per cent of our students elect their additional three months in neurology. We are grateful to our neurologists for a program which entices the student to spend his elective time in this field.

This healthy atmosphere in neurology is helpful even in the selection of students. Next year a very outstanding student is going to enter the medical school. He has been a Rhodes scholar for two years. He is interested in neurophysiology and for two summers has been at the center, seeing the opportunities of the undergraduate who is interested in neurophysiology. He now wants to take his medical training with us.

As I said before, I am interested in the better training of more neurologists. We need them to carry out our educational program in the medical school. Perhaps I am wrong, but I am even more interested in the fact that every doctor who graduates should have a sound background in this field in order that he can deliver a maximum of professional competence to his patients.

Administration of Training Programs by the National Institute of Neurological Diseases and Blindness

Gordon H. Seger, Dr.P.H.

DR. BAILEY in his presentation indicated the acute need for the training of additional personnel. Dr. DeJong and Dr. Forster have commented on what has been accomplished. I would like to describe how the institute with the aid of its civilian consultants developed and administers its training programs.

The act establishing the National Institute of Neurological Diseases and Blindness contained authorization to support the training of personnel. The first appropriation was $1,232,253 made for the fiscal year starting July 1, 1951. Of this sum, $87,400 was expended for training which served to support 15 research fellowship and 11 clinical traineeship awards. For the next fiscal year, the institute's appropriation was $1,972,300, of which $260,000 was utilized for training.

On the basis of a resolution by the National Advisory Neurological Diseases and Blindness Council, a portion of this $260,000 was used for grants to medical schools to facilitate the training of specialists for investigative careers. As a result, six grants were made, inaugurating the present Graduate Training Grant Program.

Each year Congress has seen fit to increase the amount available for the training of investigators. In recommending an appropriation of $1,950,000 solely for training for the present year, the Committee on Appropriations stated: "Programs in research on the treatment of neurological and sensory disorders, as in other areas, depend upon a supply of well trained scientific personnel. The Committee is impressed by the present critical shortage of such personnel which threatens the long range development of the research attack on these diseases. The Committee recommends an increase for training grants over and above the $96,000 increase recommended by the House in sufficient amount to permit development of a well-rounded training program in the Institute. The Committee understands that the bulk of the training funds will be made available in the form of grants to a group of non-Federal institutions that have been exceptionally productive in the training of research workers." *

This is quoted from the committee report to indicate the attitude of Con-

*Report No. 410, Committee on Appropriations, 84th Congress, Labor-Health, Education and Welfare Appropriations Bill, 1956 (HR 5046) June 2, 1955.

Chief, Extramural Programs Branch, National Institute of Neurological Diseases and Blindness, U. S. Department of Health, Education and Welfare.

gress relative to training, and also to show that funds appropriated to support the institute's training program are for the purpose of training career investigators in fields pertinent to research progress in neurologic and sensory disorders.

The Institute now administers three training grant programs, namely, research fellowships, graduate training grants, and special clinical traineeships. Each is designed to meet a specific need. Each program is flexible so as to meet the changing condition of the need.

RESEARCH FELLOWSHIPS

The purpose of the research fellowship program is to increase the number of laboratory scientists qualified to carry on independent research. Under this program three types of fellowship awards are available; the predoctoral research fellowship for those having a bachelor's degree or equivalent training; the postdoctoral research fellowship for those holding a Ph.D.; and the special research fellowship for those who have a doctoral degree in the medical sciences and, in addition, have either demonstrated unusual competence for research or require specialized training for research in a specific area.

The stipend for each type of fellowship is relatively liberal, with additional allowances for dependents, research supplies, tuition, and any travel necessary to undertake the training. The stipends for predoctoral and postdoctoral fellows are set by regulation, whereas the stipend for special fellows, in order to provide for special circumstances and conditions, is determined on the basis of qualifications and financial need.

All applications for research fellowships are referred to the Research Fellowships Central Qualifications Board of the National Institutes of Health. This board, comprised of representatives from each of the several institutes, determines the eligibility of the applicant and recommends the institute to which the application can most appropriately be referred for further consideration. Each institute, in turn, has a Research Fellowship Specialty Board, made up of scientists from the various research fields most pertinent to the central mission of the institute. This specialty board, after careful review of all evidence submitted by the applicant and information solicited from the applicant's teachers and employers, makes its recommendations to the Surgeon General for final action.

The budget for this activity for the present fiscal year is $150,000, which has sufficed to make 12 awards at the predoctoral level, 27 at the postdoctoral level, and two special fellowship awards. The number of applicants recommended for support has always been in excess of budgetary means.

GRADUATE TRAINING GRANTS

The purpose of graduate training grants is to assist institutions to increase the number of personnel available for academic and research careers in neurologic and sensory diseases, and to aid institutions in developing and improving their training programs in the departments concerned. Such grants are program grants aiding institutions to establish, expand, and improve training programs in areas where there is a recognized dearth of competent teachers and investigators. Consequently, graduate training grants are awarded primarily for training additional clinical teachers and investigators in neurology,

ophthalmology, and otolaryngology.*

Funds awarded under the graduate training grant program are to be used to supplement the institution's own financial outlay rather than as a substitute for institutional funds. The amount granted for any one program in a particular institution, therefore, varies with the need of the institution and its capacity to train. Funds may be used to employ additional staff, to provide additional residency stipends as well as to supplement existing stipends, to purchase equipment necessary for training purposes, to purchase consumable supplies, and to finance travel to enable residents to attend meetings and conferences. One other provision has been added recently to aid in recruiting likely candidates. In clinical neurology and ophthalmology, our council has authorized for each program grant the expenditure of funds to support two summer clerkships for junior or senior medical students at a maximum of $600 each. Through this mechanism a program director can often attract promising students to his department and determine the student's interest and potential for an investigative career before accepting him for a residency to be supported from grant funds.

Experience to date indicates program directors are budgeting about 75 per cent of the funds awarded under graduate training grants to support personnel, including additional staff and additional residents; 17 per cent is used for equipment, consumable supplies and travel; and the remaining 8 per cent is budgeted to cover institutional overhead costs.

*Subsequent to this report, the National Institute of Neurological Diseases and Blindness inaugurated a program of Postdoctoral Training Grants in the basic neurological sciences.

Graduate training grants are not initiated without most careful consideration, since support once started is intended to be continuous. Consequently, an application for even a relatively small sum is looked upon as potentially involving an expenditure of hundreds of thousands of dollars over a period of years. Approval is not recommended, therefore, without a rather clear understanding that every effort consistent with good school administration will be made to train teachers and clinical investigators. Grants to establish training programs or to aid those recently established are usually made for an initial period of three years. Grants to aid well established programs that have already proved themselves are usually made for a period of five years and are renewable for additional periods of five years each.

All applications for a graduate training grant are referred to a committee of nongovernmental experts for initial consideration and recommendation. These committees, comprised of consultants appointed by the Surgeon General for a specific period of time, are able to draw upon other experts to aid them in an advisory capacity on particularly perplexing problems. A training committee maintains a continual evaluation of the status of training in its particular specialty, has current information as to the number of trained personnel available, works out and advises on procedures to make training more effective, and visits institutions to aid and advise program directors, as well as to evaluate the program proposed or underway.

Almost invariably, consideration of an application for a graduate medical training grant necessitates a program site visit by one or more members of a training committee. Because the information

that can be conveyed on a written application is so limited in relation to pointing up the administrative framework within which a program operates and the facilities available for training, committee members usually wish to talk with the program director and his staff, survey the physical facilities and clinical material, and confer with institutional administrative officials. Committee members feel that only through such a visit can an objective evaluation of the potentialities for a successful program be made and the chances of an injustice in considering an application eliminated.

Probably the most frequently encountered questions during such visits are inquiries as to the characteristics of an ideal program or the ideal organization for training. Such questions are impossible to answer since the "ideal" program for any institution is that which proves to be the most effective in that particular school. No attempt is made to force programs to conform to a pattern, but rather, every effort is made to aid the institution to train competent personnel in its own particular fashion. It is believed that this philosophy is fundamental to the development and continued success of training programs aided by Federal grants.

After consideration by a training grant committee, an application is referred to the National Advisory Neurological Diseases and Blindness Council with the committee's recommendation. The function of the council is to determine whether the proposal and recommended action is within training grant policy, and to weigh the value of the proposed plan to the over-all institute program. The council then makes its recommendations to the Surgeon General, and if this action is favorable an award is made for a specific term of years. Continuation support beyond that term is determined by the success of the training program, as measured largely by the proportion of well trained individuals who choose academic or investigative careers.

The National Institute of Neurological Diseases and Blindness realizes that no program director can determine the future careers of his trainees. It believes, however, that trainees can be so chosen, so trained, so stimulated and encouraged as to increase the chances that highly competent specialists will elect to follow careers in investigative medicine.

This program is now in its third year. At present, 52 grants support training in neurology and 22 grants have been made in the field of ophthalmology. Just recently the first applications for training in otolaryngology have been received. Applications for graduate training grants may be submitted at any time and are processed as speedily as possible.

GRADUATE CLINICAL TRAINEESHIPS

The clinical traineeship program is mentioned last since it covers a type of training more advanced than that provided under graduate training grants and thus serves to complement the latter program.

Graduate clinical traineeships are of two types, the regular traineeship with a set stipend of $3,400 for the first year plus allowances for dependents and travel, and the special clinical traineeship which carries a stipend based on the applicant's qualifications and needs so that special circumstances may be met.

Regular clinical traineeships are intended to support further training of prospective investigators who have com-

pleted the requirements for a medical degree and have served the customary internship. Few awards of this type are made since this area is served by graduate medical training grants. Special clinical traineeships, on the other hand, are awarded to those who have completed the residency requirements for a specialty and wish further highly specialized training. Special clinical traineeships, for example, are awarded to neurologists who wish a year or two of neuropathology, to pediatricians who desire training in pediatric neurology, to ophthalmologists who wish training in ophthalmic pathology, and to pathologists who desire training in neuropathology. Since the stipend for a well qualified applicant is liberal, special clinical traineeships have proved to be quite valuable to institutions in training potential staff members. This program offers a somewhat broader choice of training centers since special clinical traineeships are awarded for training both in this country and abroad.

All applications for clinical traineeships are reviewed by the Neurology Institute's Traineeship Review Board. This board is made up of institute scientists who carefully review each applicant's qualifications, consider the training desired, the teacher sponsoring the applicant, and the recommendations made by authorities who are intimately acquainted with him. This board then makes its recommendation to the Surgeon General for final action. Traineeship awards are paid direct to the trainee by monthly check from the Federal government.

Funds allotted for this activity during the present fiscal year will suffice to make about 75 awards.

SUMMARY

In summary, the three training programs administered by the National Institute of Neurological Diseases and Blindness have been outlined briefly and the purpose of each indicated. Further details relative to these programs may be found in a Public Health Service brochure which has been distributed to all training institutions and research centers,* or information may be obtained by writing to the National Institute of Neurological Diseases and Blindness, Bethesda, Maryland.

These programs are subject to minor modifications to meet the changing needs for training. Such alterations as are made will be based on the advice and recommendations of program directors and civilian consultants. This conference is one of the methods used by the institute to obtain valuable guidance and counsel.

*Research and Training Grants and Awards of the Public Health Service, U. S. Department of Health, Education, and Welfare, October 1955.

Commentary on Morning Session

George Aagaard, M.D.

DR. BAKER, members of the panel, and other distinguished guests. It has been a really informative morning for me and I am sure for some of my fellow deans. I would like to add a few comments and in doing so underline what has been said so well already. I wish to express the thanks of the University of Washington for assistance received from the various grants from the National Institute of Neurological Diseases and Blindness. They have made a very important contribution to our program of teaching and research. It seems to me, as Dean Rappleye once said, "If you can bring a good teacher and a good student together, you don't have to worry too much about the outcome, regardless of the administrative framework in which the teaching is carried out." This is true in neurology as well. If we can bring good students together with teachers who are well informed in their subjects, we don't have to worry about the end result.

I would like to make my comments in connection with the undergraduate program. It is our feeling that when students complete two basic science years they are well informed on neuroanatomy, neurophysiology, neuropathology, and so on. Our problem is how can we minimize the loss of this understanding as they go through the next two clinical years and beyond. They can speak and understand the language of the neurophysiologist—they can't always do this at the end of their fourth year. To maintain students' interest in these basic fields, we have conjoint clinical conferences between the third and fourth years. More and more I have wondered if the basic science departments should have more active participation with the third and fourth year students' educational program. We have been more successful in bringing clinical departments into the first and second years, than in bringing the basic science departments into the third and fourth years.

Many of us can recall our early experiences in physical diagnosis which related primarily to examination of the heart and lungs. Now we find real emphasis on the examination of the nervous system as a part of this program. Our division of neurology participates very actively in this program. Clinical neurologists have an opportunity during the third and fourth years to reinforce the basic science taught during the first two years. We have been happy to see a real conjoint effort on the part of neurology and neurosurgery develop. Next year arrangements have been proposed

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and approved by the Executive Committee so that clerkships will be organized in such a way that most of our students will have their service on neurology and neurosurgery as one unit. This will give much greater impact with cooperative efforts of both of these divisions over a continuous period of time. At our school, neurology also teaches on beds in the pediatric wards. This is a step in the right direction.

How can we increase the impact of neurologists in the teaching of clinical neurology? I would like to introduce one thought. Is it not possible that we can make an even greater impact by having closer liaison with other clinical departments in the medical school? I wonder if we can also have an impact in this direction by having teachers of neurology have closer participation in medical grand rounds, in pediatrics, in psychiatry, and so on. At present we don't have enough people, but as we get more, is it possible that the presence of a neurologist on medical and pediatric grand rounds will have an impact on our teachers of internal medicine and pediatrics. Since it appears that it will be a long time before there will be adequate numbers of teachers in neurology as a specialty to do the necessary teaching job, can we use teachers of internal medicine, pediatrics, and psychiatry to help with this important task?

It is heartening to notice that 92 of the residents trained on the training grants program were from fields other than neurology. Many of these men are going into teaching in fields other than neurology, but they still will have a great impact on their students regardless of their field of interest.

While one can agree with the need for having in the department of neurology people who are trained in neuroanatomy, neurophysiology, neurochemistry, and so on, there are dangers that, if we have a closely knit unit active in research and self-sufficient within itself, we may have a lack of cooperation with other fields. We need people who have retained a contact with some other department.

Finally, I would like to say just a word about a problem which concerns me in administration. It is the problem of space. All of us have been heartened by the increasing support available and the increasing tendency to give long term support for teachers and investigators. Many of us in medical schools are concerned about finding a place where we can put these people to work – office space – laboratory space. We are encouraged by optimistic reports on bills before the Congress now. Here again is an area in which we can all unite in an effort which will in turn have its effect on this program in which we are so interested this morning.

PANEL DISCUSSION

Problems Encountered in Neurologic Education

1. WHAT DO YOU CONSIDER AN IDEAL TRAINING PROGRAM IN NEUROLOGY?

DR. HOUSTON H. MERRITT: I think I can enumerate the ideals. They will probably not be attained at any one place. 1) Adequate patient material, that is, an independent neurologic service with inpatient and outpatient facilities. 2) Therapeutic responsibility by the resident for his patients. 3) A sufficient number of teachers in both clinical and basic sciences. 4) A service that is associated with a medical center where it can have ready access to other services, particularly medicine, pediatrics, psychiatry, neurosurgery, orthopedics, otolaryngology, and so on. 5) A service that is part of a medical school. Such a service would then have intimate connection with the departments of anatomy, pathology, physiology, biochemistry, and pharmacology. In my opinion, it is not essential that those teachers of the basic sciences related to neurology be in the department of neurology. The neuropatholigst, for example, can be in the department of pathology, assigned to neurology, but I think he should be considered a part of the neurologic service. The same way with the anatomist. He should have an appointment with anatomy and be assigned to neurology. The same with the biochemist and pharmacologist.

This is the ideal. In some centers where the hospital size is not sufficient to give neurology an independent service, it has to be worked out in another manner. In such institutions it may be necessary to develop neurology in a medical or psychiatric service. This is possible only if the chief of that service has a sympathetic ear to the needs of the neurologist and the chief of neurology can have direct access to the dean in administrative matters related to his service. If the school cannot provide a special man in pathology assigned to the neurology service, then it may be necessary to encourage the training of a man in the pathology department to work with the neurologic unit. This same procedure could be employed in the development of physiology, anatomy, biochemistry, and the like. It may take consultation with other services to get them to realize the importance of this type of program, but I think it can be done.

DR. RUSSELL N. DEJONG: I quite agree with Dr. Merritt's comments. It is not essential to have pathology, neurophysiology, and so on under the department of neurology. However, it certainly helps. There are very few schools where neuroanatomy is under neurology. Ideally, I feel that it should be, because of the clinical applications of neuroanatomy. There are many centers where there is not only the problem of having a satisfactory basic science correlation, but where, due to precedent, there is not even a specific and distinct neurology

service and the neurologists have no beds of their own and merely act as consultants to the other services. This type of arrangement is a very difficult one and the entire philosophy of the school or the department in charge must be changed to improve the neurologic setup.

DR. FRANCIS M. FORSTER: A department of clinical neurology devoid of contact with or orientation in research in any or all related fields is a department in name only. Actually this can be arranged in many ways; for example, at Georgetown University the department of biochemistry is not particularly oriented toward research in neurochemistry. The department of neurology, therefore, has developed a neurochemist who works in biochemistry under both departments. He thus aids in the teaching of both departments. This has worked out very well. It has strengthened the school and has also strengthened the research program of the department of biochemistry. I also do not feel that a neurology service should necessarily have all facilities that deal with the nervous system. Few departments could develop such a staff.

DR. HAROLD S. DIEHL: I agree with what Dr. Merritt and the others in the panel have said. I think at Minnesota we meet most of the points mentioned. I should like to emphasize one other consideration for inclusion in an ideal and successful program in neurology. This is dynamic leadership of the field in the department. That type of leadership will make a neurologic program progress and develop in the school.

2. WHAT ARE THE IDEAL ADMINISTRATIVE CONDITIONS WHICH NEED TO EXIST TO RUN AN EFFECTIVE TRAINING PROGRAM?

DR. JAMES O'LEARY: The most important administrative setup for any service is that the neurologist-in-chief should have autonomy of neurologic beds, and in the medical school he should have direct access to the dean's office with respect to the solicitation of outside funds, budget matters, and space requirements.

DR. FORSTER: Wherever it is feasible in the structure of the medical school, it is advantageous for the department head to be on the policy-making board. I am sure there may be a fair amount of difference with that opinion.

DR. MERRITT: I think one has to remember that the department of neurology is in competition with every other department in the medical school. However, every medical school has rules as to who should serve on the board and committee. It would be impossible for every service to do so.

3. WHAT CONDITIONS ON A MEDICAL SERVICE SHOULD BE UNDER THE CARE OF A NEUROLOGIST?

DR. FORSTER: That depends largely on the institution and the hospital. Certain problems such as brain tumors and the degenerative diseases of the nervous system offer no problem. The real problem arises when one considers such illnesses as vascular disturbances, myasthenia gravis, meningitis, polio. Just how many of these will be cared for by neurology will depend upon how the department is structured and the particular interest in the department. Everyone will agree that an epileptic patient should not be assigned to the medical service when there is a capable department of neurology. In many cases the policy will be determined at the particular institution.

DR. DEJONG: It is very difficult to generalize. Any patient whose illness is primarily due to involvement of the central

or peripheral nervous system, whether it be inflammatory, vascular, neoplastic, or degenerative, should be under the care of the neurologist. There are overlaps, I know, in many institutions and in many conditions. I feel that cerebrovascular disease is better treated by a neurologist if at all possible. At our own hospital those inflammatory diseases of the nervous system under contagious precautions are not taken care of by a neurologist. Ideally, however, they should be under the care of a neurologist, also. There are borderline cases where one is dealing with neurologic complications of systemic disease of various types, and in some instances of this sort the case may be cared for jointly by the neurologist and a specialist in some other field.

DR. MERRITT: At our hospital, the neurology service cares for most conditions generally classified as neurologic. We share the infectious diseases such as meningitis with the medical service. We share polio with the pediatric service. We handle myasthenia gravis and the collagen diseases that affect the nervous system. Blood dyscrasias are treated in consultation with the hematology service.

This whole problem really evolves around the presence or absence of a physician who has an interest in these diseases. In many places, neurology has no interest in polio or in infectious diseases. The neurologist himself determines the type of patient he takes care of.

DR. PEARCE BAILEY: I was brought up under the general concept that the neurologist was the only good general practitioner left.

DR. A. B. BAKER: Would the panel care to comment on the impact of the type of material on the training program? Without the proper range of material for treatment, how can you indoctrinate the neurologic trainee to do anything besides fancy clinical diagnosis?

DR. DEJONG: I am not certain just how to answer the question as you have asked it. Of course, the neurologist certainly should be prepared to take care of all the problems mentioned and additional ones too, because if he is to go out into practice he will be asked to serve as a consultant. Another solution to this problem of patient material is something that was mentioned this morning – cutting across departmental lines, which I think is an important part of the training of the neurologist. Some of these problems may not be taken care of in the neurology service in a particular institution. If the neurologist can see these patients on another service and act as a consultant, it broadens his training. There may also be neurologic problems in which therapy is beyond the training of the average neurologist. He can further his training by having consultants from other services carry on with him. For example, consider anticoagulant therapy. In our institution we have a team. They are well organized with a good laboratory setup. We usually call in this anticoagulant team when necessary. Nevertheless, the neurology resident is in charge of the patient and works closely with that team and learns how to manage these cases, although he does not have complete responsibility. The same thing happens in other diseases. We have quite a few diabetics. Sometimes we get them because they are too much trouble to take care of on the regular service. Sometimes the neurologist, with the help of an endocrinologist, can manage the case. This increases his therapeutic ability and gives additional contact with other problems for which he acts as a consultant.

4. CAN A RESIDENT BE TRAINED IN NEUROLOGY WITHOUT HAVING TOTAL PATIENT RESPONSIBILITY?

DR. MERRITT: Dr. Bailey discussed this a few minutes ago. The answer is no. He cannot be trained unless he has responsibility for therapeutic care of the patient. He may get guidance from his superiors in the residency training program and attending physician. He can follow some of these patients on a long term basis in the outpatient clinic. Only by following his own patients can he see how effective treatment is and how it should be modified.

DR. AUGUSTUS S. ROSE: I would answer this question in the same manner as Dr. Merritt, but I would qualify it. Under certain circumstances, in certain institutions, and in certain hospitals, it might be possible for a resident to be trained for a period of time without a separate neurologic service in which there are beds which he controls. However, it is not possible to have an adequate residency program without separate beds and bed responsibility if it is to be carried on for any period of time. I do not believe a good program can exist under these conditions.

5. WHAT ARE THE DISADVANTAGES OF HAVING A SCATTERED NEUROLOGY SERVICE IN THE HOSPITAL SETUP?

DR. DEJONG: There are many disadvantages. If the resident is to have complete responsibility for his patients, and I feel strongly that he should have, it is very difficult for him to follow these patients closely, to be in intimate contact with them at all times, if they are scattered all over a large hospital. If he has all his patients on one ward, the nurses will be familiar with the many special neurologic diseases and procedures and will thus enable their patients to be cared for more efficiently. Certainly a great deal of time will be saved if the patients are in one geographic area. The practice of neurology is time consuming, and to ask a resident to take care of his patients in scattered areas of the hospital contributes to inefficiency. It creates many problems, particularly with reference to observation, as well as the management of therapeutic programs.

DR. O'LEARY: We have one outstanding example in our private neurologic service of the amount of time saved when patients are in one area. Our resident formerly spent four to six hours in making ward rounds – now it takes him an hour and 45 minutes on the segregated system.

6. WHAT IS THE ROLE OF THE OUTPATIENT CLINIC IN A GRADUATE TRAINING PROGRAM?

DR. RICHARD B. RICHTER: The answer must vary to some extent from one training unit to another, depending on how large the unit is. In our hospital the outpatient service is especially large in proportion to the hospital service. We are inclined to use it heavily in our teaching, with great advantage. It is not only the size that determines its teaching value, but the manner in which it is staffed and the way it is integrated with the hospital service. We are quite favorably situated in this regard and are able to utilize it quite effectively for teaching. The attending staff of the outpatient clinic is identical with that of the hospital service. No part of the personnel assigned to outpatient is not actively working in the hospital. Our hospital patients are admitted through the neurologic outpatient clinic. An equally large portion return for care after having

been in the hospital. This makes it possible for the residents to see the patient on the initial visit to the clinic where he often takes the history, and to follow him to the hospital and back to the outpatient clinic for subsequent observation and care which may extend over some years. It is this opportunity to follow through over a considerable period of time that is the most important feature of the outpatient clinic in teaching graduate students clinical neurology. There are other important advantages. Obviously it is only in an outpatient clinic that the resident has an opportunity to get wide acquaintance with a number of neurologic conditions that do not require hospitalization, such as epilepsy, myasthenia gravis, parkinsonism, and so on. It is an ideal place to begin to give responsibility to the resident in the care of patients.

DR. MERRITT: The doctor-patient relationship is more real in the care of an outpatient than any other place in the resident-patient setting. There is an artificial division of responsibility between the junior resident, senior resident, and staff as soon as the patient enters the hospital.

DR. ROSE: In a residency training program, the outpatient department is so essential that it should not be called a residency training program without an outpatient service. It is often possible to have a good training program without separate inpatient beds, provided there is a good outpatient department. If this is not possible, then an adequate training program could not be provided.

7. HOW AND WHY SHOULD ELECTROENCEPHALOGRAPHY BE INTEGRATED IN A NEUROLOGY TRAINING PROGRAM?

DR. O'LEARY: I would ask you to consider internal medicine and cardiology and its relationship to the electrocardiogram. No one would consider turning out a cardiologist or an internist without a knowledge of electrocardiology. A neurologic resident, therefore, should learn to read electroencephalograms and to know variations occurring in childhood, old age, convulsive disorders, and various other uses. To become competent to handle electroencephalography as an adjunct to his patient work-up, a neurologic resident should spent four to six months in the laboratory actively working with the various technics and reading many tracings under the guidance of competent staff.

To become a good electroencephalographer and be competent to handle a laboratory would require complete neurologic training, plus a minimum of one year's training in the laboratory. There are too few neurologists who are competent to establish a laboratory and teach electroencephalography. Special fellowships should be set up for this purpose.

DR. DEJONG: I would like to add that I agree in general with what Dr. O'Leary has said. I know he is much more oriented toward electroencephalography than I am. The neurology trainee should spend time in the laboratory and apply electrodes. He should supervise recording as well as reading. This is important in neurologic training because in many clinics the neurologist must not only run the neurologic service, but must also supervise the electroencephalography laboratory. We know that electroencephalography services have expanded throughout the country, and in many hospitals they are run by technicians, pathologists, physiologists, and psychologists. This is unfortunate since it es-

tablishes the electroencephalogram as a laboratory technic run by a person with no clinical background, who then also interprets the findings in terms of neurologic deficit.

8. HOW LONG DOES IT TAKE TO TRAIN A GOOD NEUROLOGIST?

DR. ROSE: Certainly five years of training, including at least one year of internal medicine, would be ideal.

DR. DEJONG: It is an individual problem. I think it has been the experience of all of us that good men have not left at the end of three years. They have stayed for four or five years. To get the fundamentals, three years is a minimum. A good man will see that he gets four or five years. Three years is the prescribed standard, and most of the men who have three years of training plus two years of practice will get through the board examinations all right and will be pretty good clinicians.

DR. MERRITT: The requirements of the board are quite good, calling for three years of training and two years of experience. Many men stay in the hospital for two years for further training. Most of them get sufficient training to be good neurologists. It takes about five years.

DR. ROSE: Another point of discussion is the matter of the board requirements. I would like to say, as a member of a staff on a university, I agree with my university that I do not believe the specialty boards should decide what a university should require for training. I believe that the training and requirements should be at the university level. I would like to think the specialty boards are to examine and not to set standards.

DR. DEJONG: When criteria are established by the specialty boards, they are minimum criteria. There has to be some arbitrary statement. The board can't merely say that it requires adequate training in neurology. The board, I am sure, does not in any way try to influence schools or tell them how they should train. I am on the residency training committee of the A.M.A. and the board and I receive letters asking what should be done in establishing a training program. Every program is an individual one, but the board does not state how any single program should be organized.

DR. MERRITT: This matter of qualification bothers me on all levels of education. No medical school sets out to train men to pass the board, but if 50 per cent fail, they should sit up and ask why.

9. HOW MUCH SHOULD WE USE OUR PART TIME UNPAID FACULTY IN THE TRAINING OF CLINICAL NEUROLOGY?

DR. MERRITT: Part time faculty in practice can bring to the students a viewpoint which a full time man often does not have. Many are just as capable teachers as those on the full time staff. I do not think you could run a good service without some full time men, but the part time, unpaid or paid, faculty contribute a great deal. Of course, it is a matter of selecting those who are capable of teaching and capable of keeping up with advancements.

DR. BAKER: How reliable are part time men in a teaching program?

DR. MERRITT: In our large cities this is not a problem, as it may be in smaller communities. A colleague can take the place of a man who is called away. Most practitioners accept this responsibility just as seriously as if they were getting $10,000 to $15,000 a year for it. Those who chronically do not attend to their

duties are not reappointed.

10. IN A WELL PLANNED PROGRAM, HOW MUCH TIME SHOULD BE SPENT IN LABORATORIES AND IN BASIC NEUROLOGY?

DR. FORSTER: This depends on the program. In my three-year residency program we set aside six months for basic work. The last six months are elective and determined in part by the trends and the interest of the residents, as well as what the program has to offer.

DR. DEJONG: In the training of a clinical neurologist, the resident must spend the larger portion of his time in clinical work with patients on the wards and in the outpatient department. I feel that in those programs where the resident spends a larger portion of his time in laboratories and in research, he does not come out as a well rounded neurologist.

11. WHAT ARE THE OPPORTUNITIES IN THE FIELD OF NEUROLOGY TODAY?

DR. AURA E. SEVERINGHAUS: This is a problem which faces education at every stage. What are the opportunities in neurology at present and what is the promise for the future?

DR. BAILEY: The opportunities are unlimited. There are very great opportunities in research, which, of course, is my main interest. We spoke this morning about the great rise in experimental neurology. There is also a great need in clinical situations. There is great need for teachers. Only a small portion of the medical schools in this country can meet adequate criteria for teaching faculty in neurology, and by that I do not mean rigid criteria, but actual operating criteria of turning out trained neurologists who are trained on the basis of assuming therapeutic responsibility. There is great opportunity for medical leadership in neurology. If neurology deals with the central mechanism for all refined human movements and activity, why is it there are not more neurologists as medical leaders? There used to be in the past. I think if we get these national training programs really going and we get together in conferences such as this, we will be able to point to leaders in medicine who are actually neurologists.

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and streptococcic infections. At the present time, they said, ristocetin can be administered to patients only by vein because injections of the antibiotic are painful and oral dosages do not provide sufficient concentrations to be effective. Further research will attempt to evaluate the extent to which it could find general or special use in medicine.

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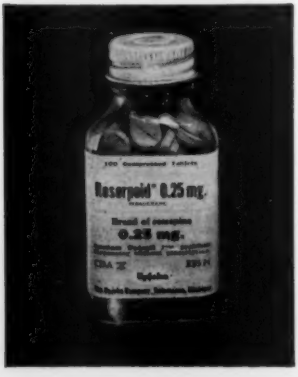

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DECEMBER, 1956

Title Deadlines For AAN Meeting January 11, 1957 is the deadline for submission of titles and abstracts of scientific papers and demonstrations to be presented at the ninth annual meeting of the American Academy of Neurology to be held at the Sheraton Plaza Hotel in Boston (April 22-27, 1957) .... Titles and abstracts (not to exceed 150 words) should be forwarded to the scientific program director, Dr. James L. O'Leary, Division of Neurology, Washington University, School of Medicine, St. Louis 10, Mo.... Titles and 150-word abstracts of demonstrations or exhibits should be sent to Dr. Louis D. Boshes, Department of Neurology and Psychiatry, Northwestern University Medical School, 303 East Chicago Avenue, Chicago 11, Ill.... If motion pictures are to be shown, whether as part of papers-from-platform or of demonstrations, the film size, sound requirements, or special projection needs should be indicated.

AAN Registry For Positions Maynard M. Cohen announces that staff work has been completed for the AAN registry of vacant positions in neurologic teaching, research, and practice. Qualified physicians or scientists in such positions should write Dr. Cohen. Similarly, universities and other institutions, or physicians in private practice wishing to procure individuals trained in clinical neurology or the neurologic sciences, also should make their needs known to the registry. All inquiries and related correspondence will be kept confidential. Interested individuals or institutions may write Dr. Maynard M. Cohen at the University of Minnesota, Minneapolis 14, Minnesota.

Magoun to Give Wechsler Lecture Horace W. Magoun, professor of anatomy at the University of California School of Medicine in Los Angeles, will give the annual Israel S. Wechsler lecture at the Mount Sinai Hospital of New York City. His topic is: "Aristotelian Psychology and the Twentieth Century Brain."

85 Added to AAN Membership In October Passing September's peak of 79 new members, 85 additional physicians and scientists have accepted invitations to AAN membership. These new members (all categories) are: George L. Alexander, Jr., Richard J. Allen, L. M. N. Bach, John B. Baker, Antonio Becerra, Aaron Bell, William E. Bell,

Arthur L. Benton, Nicholas A. Bercel, William Berenberg, Reginald G. Bickford, Milforde Blackwell, Virgil Boekelheide, Herbert L. Borison, James F. Bosma, Joseph V. Brady, Theodore H. Bullock, James B. Campbell, Malcolm B. Carpenter, Hsiang-Tung Chang, Kao Liang Chow, Nicholas Christoff, George W. Corner, Erminio Costa, Chester W. Darrow, Edward H. Davis, Remzi Demir, Robert A. deNapoli, A. J. Derbyshire, John B. Doyle, Charles E. Edwards, Emanuel H. Feiring, J. Folch-Pi, W. Horsley Gantt, Robert S. Graham, Peter Gruenwald, H. K. Hartline, Alexander S. Hartman, William K. Hass, Williamina A. Himwich, Ebbe C. Hoff, William E. Kelly, Nathaniel Kleitman, John R. Knott, Stanley S. Lamm, Wilbur L. E. Larson, Henry R. Liss, D. L. Lloyd-Smith, Niels L. Low, Elliott L. Mancall, Franklin Martin, Jr., Warren S. McCulloch, Gilbert W. Meier, J. Mendelson, Blaine S. Nashold, Jr., Juan Negrin, Jr., Charles R. Noback, Walter D. Obrist, Pedro Pasik, Tauba Pasik, Talmage L. Peele, Esra Petursson, Dominick P. Purpura, Max Ramirez de Arellano, Ralph M. Reitan, Nelson G. Richards, Walter F. Riker, Franco Rinaldi, Arthur J. Rioepelle, Albert Schatz, Otto H. Schmitt, Julia Schneider, Gordon M. Schoepfle, John S. Scott, Richard L. Sidman, Charles W. Simpson, Ruth E. Stauffer, Hans-Lukas Teuber, Howard J. Tucker, C. S. Ushiro, Arthur G. Waltz, James MacD. Watson, Richard A. Weaver, Paul A. Weiss, and Hans J. Zwang.... Since the campaign for a larger and broader AAN membership began in the month of May, 466 physicians and scientists have been added to the rolls of membership as of Oct. 31. In this new group are 43 fellows and active members, 101 junior members, 300 associate members, and 22 honorary-corresponding members.... Inquiries on AAN membership should be sent to Dr. Pearce Bailey, Chairman, AAN Membership Committee, National Institute of Neurological Diseases and Blindness, Bethesda 14, Md.

Ivy League Kicks Off NINDB Collaborative Program

Yale and Brown universities were the first of a dozen or more institutions to receive grant awards from the National Institute of Neurological Diseases and Blindness under its expanding program for a collaborative, comprehensive attack on cerebral palsy, mental retardation, and other neurologic sequelae of the perinatal period (See Newsletter, May 1955). Yale's grant for the first year is $107,799; Brown University is receiving $97,633. These two grants mark the beginning of a concerted, multi-institutional and multidisciplinary research activity which, during the next 10 to 20 years will attempt to identify the biologic factors of the perinatal period responsible for the current high rate of fetal and neonatal mortality on the one hand and on the other for cerebral palsy, and types of deafness, blindness, epilepsy, and mental retardation. When the full roster of participating medical institutions has been achieved, it is expected that 6,000 pregnant women, infants, and children will be studied annually in terms of uniform scientific

criteria. In the collaborative scheme, the NINDB serves as a central laboratory and coordination center for the participating institutions.... The study at the Yale University School of Medicine is to be conducted by Gilbert H. Glaser, associate professor of neurology, C. Lee Buxton, professor of obstetrics and gynecology, and Milton J. E. Senn, Sterling professor of pediatrics and psychiatry. The Brown project, which embraces five local hospitals and clinics, is under the administrative direction of the university's professor of biology, J. Walter Wilson.

Cerebral Vascular Conference Held at Bethesda

More coordinated research on cerebral vascular disease is in the making, if a two-day conference, held recently in Bethesda, represents a new trend of interest. On Oct. 29-30, under the auspices of NINDB's National Advisory Council a group of 26 neurologists, neurosurgeons, and basic scientists convened to develop better criteria for the evaluation of treatment of subarachnoid hemorrhage and intracranial aneurysms. The sessions began with a consideration of such basic concepts as clinicopathologic classifications (C. H. Millikan); embryology and anatomy of the circle of Willis (L. B. Arey); topographic localization (J. L. Pool); pathogenesis (G. H. Margolis); cerebral circulation (L. Sokoloff); and the role of hypertension (L. Terry); and then passed to a discussion of clinical criteria and factors of prognosis (A. L. Sahs and H. H. Hyland). Next the program concerned itself with factors influencing the course of intracranial aneurysms, e.g. medical (J. W. Magladery and C. M. Fisher) and surgical (O. Sugar, E. H. Botterell, W. H. Sweet, and Barnes Woodhall).... On the evening of the first day the conferees were divided into three committees to formulate a protocol of uniform clinicopathologic criteria for use in projected cooperative studies on aneurysms among several medical research centers. In the morning of the second day the committee conclusions were presented: R. D. Adams for the committee on medical criteria; W. B. Hamby for the committee on surgical criteria; and H. G. Schwartz for the committee on new avenues for cooperative research. The biostatistical aspects of studies on aneurysms were given by G. H. Beebe and the conference terminated with summaries by H. Houston Merritt and A. E. Walker.... The inspiration to hold the conference came from A. E. Walker, supported by an expression of interest in the problem by the Journal of Neurosurgery, the American Academy of Neurological Surgery, and the American Academy of Neurology.

Archives Italiennes de Biologie To Resume Publication

After an interruption of 20 years, the Archives Italiennes de Biologie will resume publication in 1957 under the editorship of Giuseppe Moruzzi, professor of physiology at the University of Pisa. Founded in 1882 by A. Mosso of Turin and V. Aducco of Pisa, the first 94 volumes of the Archives pro-

vided an important channel for Italian contributions to the biologic sciences, containing the original works of Bizzozero, Golgi, Grassi, Luciani, Marchi, Mingazzini, and Mosso. Resuming with volume 95, the journal is now to publish four numbers per annum, devoted to original contributions to physiology written in either French or English.... Communications should be sent to: The Administration, Archives Italiennes de Biologie (F. Vallerini - "Sala delle Stagioni"), Lungarno Pacinotti 1, Pisa, Italy.

Tribute to Foster Kennedy Under the sponsorship of the Social Service Auxiliary to Bellevue Hospital, colleagues and friends of the late Dr. Foster Kennedy are raising a fund for building a canteen at Bellevue Hospital Center, as a memorial. Any profits which accrue from this project will be used to further the work of the Auxiliary. It is proposed to erect a plaque in Dr. Kennedy's memory, inscribed: "In Tribute to Foster Kennedy, M.D., F.R.S. (Edin) D.Sc., Director of the 2nd Medical Neurological Division 1919-1949, a great teacher, an eminent clinician and a zestful trusted friend." Contributions may be sent to Social Service Auxiliary to Bellevue Hospital, Room 11, Bellevue Hospital, New York 16.

Briefs The usual packed series of national meetings are scheduled to take place in New York City during the first part of December: the American League Against Epilepsy at the Roosevelt Hotel (Dec. 6), Association for Research in Nervous and Mental Disease at the same hotel (Dec. 7 and 8), and the examinations of the American Board of Psychiatry and Neurology (Dec. 10 and 11). Interspersing these professional society meetings: the Medical Board of the Myasthenia Gravis Foundation has an annual dinner meeting at the Roosevelt Hotel (Dec. 7), and the 21st semiannual meeting of the Medical Advisory Board of the National Multiple Sclerosis Society will be held at the Hotel Biltmore (Dec. 9).... A distinguished guest of the A.R.N.M.D. meeting will be Prof. F. Bremer of Brussels.... A recent visitor to the U.S. as a consultant to the Armed Forces Institute of Pathology was Prof. Klaus-Joachim Zulch, neurologist at the Max Planck Institute, Cologne, Germany. His major interests are cerebral edema, vascular disturbances, and the diagnosis and classification of brain tumors in adults and children.... According to a recent issue (Oct. 1956) of the Johns Hopkins University Circular (School of Medicine), a joint Committee on Neurological Disorders has been established at this medical school. Dr. A. McGehee Harvey, professor of medicine, is chairman. Dr. J. W. Magladery, associate professor of neurology, and Dr. Vernon B. Mountcastle, associate professor of physiology, are the other members of the committee.

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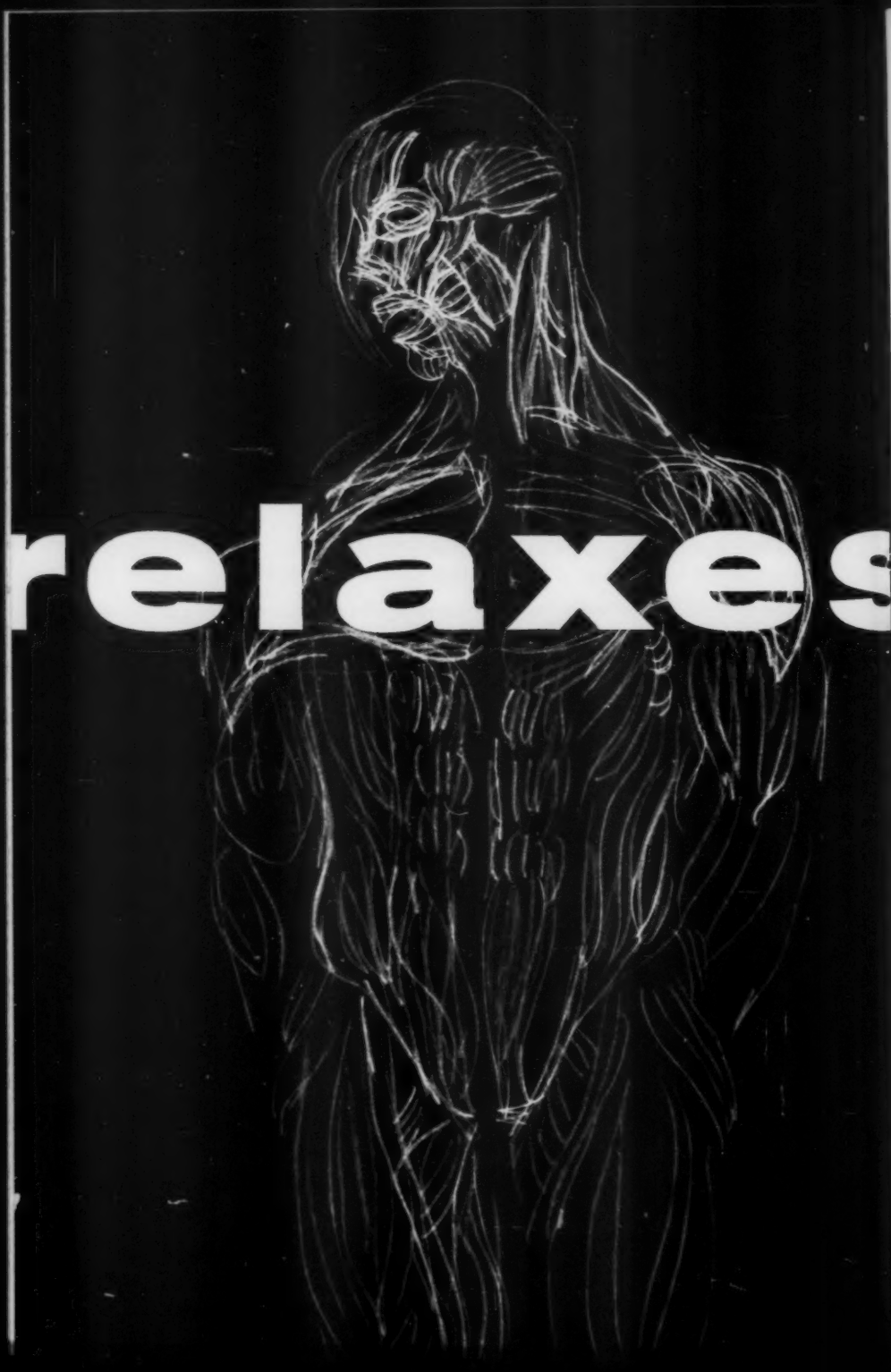
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(1) Rodriguez-Gomez, M.; Valdes-Rodriguez, A., and Drew, A. L.: J.A.M.A. 160:752 (Mar. 3) 1956.
(2) Abrahamsen, E. H., and Baird, H. W., III: J.A.M.A. 160:749 (Mar. 3) 1956.

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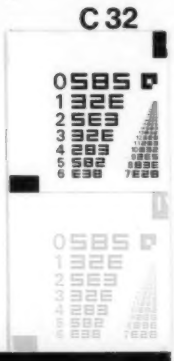
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